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Method and nucleic acids for the improved treatment

of breast cell proliferative disorders

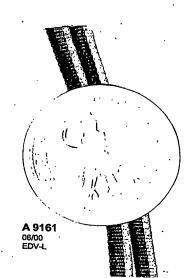
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> München, den 2. November 2005 **Deutsches Patent- und Markenamt** Der Präsident Im Auftrag

> > Schmidt C.



Method and nucleic acids for the improved treatment of breast cell proliferative disorders

Field of the Invention

The levels of observation that have been studied by the methodological developments of recent years in molecular biology, are the genes themselves, the translation of these genes into RNA, and the resulting proteins. The question of which gene is switched on at which point in the course of the development of an individual, and how the activation and inhibition of specific genes in specific cells and tissues are controlled is correlatable to the degree and character of the methylation of the genes or of the genome. In this respect, pathogenic conditions may manifest themselves in a changed methylation pattern of individual genes or of the genome.

DNA methylation plays a role, for example, in the regulation of the transcription, in genetic imprinting, and in tumorigenesis. Therefore, the identification of 5-methylcytosine as a component of genetic information is of considerable interest. However, 5-methylcytosine positions cannot be identified by sequencing since 5-methylcytosine has the same base pairing behaviour as cytosine. Moreover, the epigenetic information carried by 5-methylcytosine is completely lost during PCR amplification.

A relatively new and currently the most frequently used method for analysing DNA for 5-methylcytosine is based upon the specific reaction of bisulfite with cytosine which, upon subsequent alkaline hydrolysis, is converted to uracil which corresponds to thymidine in its base pairing behaviour. However, 5-methylcytosine remains unmodified under these conditions. Consequently, the original DNA is converted in such a manner that methylcytosine, which originally could not be distinguished from cytosine by its hybridisation behaviour, can now be detected as the only remaining cytosine using "normal" molecular biological techniques, for example, by amplification and hybridisation or sequencing. All of these techniques are based on base pairing which can now be fully exploited. In terms of sensitivity, the prior art is defined by a method which encloses the DNA to be analysed in an

agarose matrix, thus preventing the diffusion and renaturation of the DNA (bisulfite only reacts with single-stranded DNA), and which replaces all precipitation and purification steps with fast dialysis (Olek A, Oswald J, Walter J. A modified and improved method for bisulphite based cytosine methylation analysis. Nucleic Acids Res. 1996 Dec 15;24(24):5064-6). Using this method, it is possible to analyse individual cells, which illustrates the potential of the method. However, currently only individual regions of a length of up to approximately 3000 base pairs are analysed, a global analysis of cells for thousands of possible methylation events is not possible. However, this method cannot reliably analyse very small fragments from small sample quantities either. These are lost through the matrix in spite of the diffusion protection.

An overview of the further known methods of detecting 5-methylcytosine may be gathered from the following review article: Rein, T., DePamphilis, M. L., Zorbas, H., Nucleic Acids Res. 1998, 26, 2255.

To date, barring few exceptions (e.g., Zeschnigk M, Lich C, Buiting K, Doerfler W, Horsthemke B. A single-tube PCR test for the diagnosis of Angelman and Prader-Willi syndrome based on allelic methylation differences at the SNRPN locus. Eur J Hum Genet. 1997 Mar-Apr;5(2):94-8) the bisulfite technique is only used in research. Always, however, short, specific fragments of a known gene are amplified subsequent to a bisulfite treatment and either completely sequenced (Olek A, Walter J. The pre-implantation ontogeny of the H19 methylation imprint. Nat Genet. 1997 Nov;17(3):275-6) or individual cytosine positions are detected by a primer extension reaction (Gonzalgo ML, Jones PA. Rapid quantitation of methylation differences at specific sites using methylation-sensitive single nucleotide primer extension (Ms-SNuPE). Nucleic Acids Res. 1997 Jun 15;25(12):2529-31, WO 95/00669) or by enzymatic digestion (Xiong Z, Laird PW. COBRA: a sensitive and quantitative DNA methylation assay. Nucleic Acids Res. 1997 Jun 15;25(12):2532-4). In addition, detection by hybridisation has also been described (Olek et al., WO 99/28498).

Further publications dealing with the use of the bisulfite technique for methylation detection in individual genes are: Grigg G, Clark S. Sequencing 5-methylcytosine residues in genomic DNA. Bioessays. 1994 Jun;16(6):431-6, 431; Zeschnigk M, Schmitz B, Dittrich B, Buiting K, Horsthemke B, Doerfler W. Imprinted segments in the human genome: different DNA methylation patterns in the Prader-Willi/Angelman syndrome region as determined by the

genomic sequencing method. Hum Mol Genet. 1997 Mar;6(3):387-95; Feil R, Charlton J, Bird AP, Walter J, Reik W. Methylation analysis on individual chromosomes: improved protocol for bisulphite genomic sequencing. Nucleic Acids Res. 1994 Feb 25;22(4):695-6; Martin V, Ribieras S, Song-Wang X, Rio MC, Dante R. Genomic sequencing indicates a correlation between DNA hypomethylation in the 5' region of the pS2 gene and its expression in human breast cancer cell lines. Gene. 1995 May 19;157(1-2):261-4; WO 97/46705, WO 95/15373, and WO 97/45560.

An overview of the Prior Art in oligomer array manufacturing can be gathered from a special edition of Nature Genetics (Nature Genetics Supplement, Volume 21, January 1999), published in January 1999, and from the literature cited therein.

Fluorescently labelled probes are often used for the scanning of immobilised DNA arrays. The simple attachment of Cy3 and Cy5 dyes to the 5'-OH of the specific probe are particularly suitable for fluorescence labels. The detection of the fluorescence of the hybridised probes may be carried out, for example via a confocal microscope. Cy3 and Cy5 dyes, besides many others, are commercially available.

Matrix Assisted Laser Desorption Ionization Mass Spectrometry (MALDI-TOF) is a very efficient development for the analysis of biomolecules (Karas M, Hillenkamp F. Laser desorption ionization of proteins with molecular masses exceeding 10,000 daltons. Anal Chem. 1988 Oct 15;60(20):2299-301). An analyte is embedded in a light-absorbing matrix. The matrix is evaporated by a short laser pulse thus transporting the analyte molecule into the vapour phase in an unfragmented manner. The analyte is ionised by collisions with matrix molecules. An applied voltage accelerates the ions into a field-free flight tube. Due to their different masses, the ions are accelerated at different rates. Smaller ions reach the detector sooner than bigger ones.

MALDI-TOF spectrometry is excellently suited to the analysis of peptides and proteins. The analysis of nucleic acids is somewhat more difficult (Gut I G, Beck S. DNA and Matrix Assisted Laser Desorption Ionization Mass Spectrometry. Current Innovations and Future Trends. 1995, 1; 147-57). The sensitivity to nucleic acids is approximately 100 times worse than to peptides and decreases disproportionally with increasing fragment size. For nucleic acids having a multiply negatively charged backbone, the ionization process via the matrix is

considerably less efficient. In MALDI-TOF spectrometry, the selection of the matrix plays an eminently important role. For the desorption of peptides, several very efficient matrixes have been found which produce a very fine crystallization. There are now several responsive matrixes for DNA, however, the difference in sensitivity has not been reduced. The difference in sensitivity can be reduced by chemically modifying the DNA in such a manner that it becomes more similar to a peptide. Phosphorothioate nucleic acids in which the usual phosphates of the backbone are substituted with thiophosphates can be converted into a charge-neutral DNA using simple alkylation chemistry (Gut IG, Beck S. A procedure for selective DNA alkylation and detection by mass spectrometry. Nucleic Acids Res. 1995 Apr 25;23(8):1367-73). The coupling of a charge tag to this modified DNA results in an increase in sensitivity to the same level as that found for peptides. A further advantage of charge tagging is the increased stability of the analysis against impurities which make the detection of unmodified substrates considerably more difficult.

Genomic DNA is obtained from DNA of cell, tissue or other test samples using standard methods. This standard methodology is found in references such as Fritsch and Maniatis eds., Molecular Cloning: A Laboratory Manual, 1989.

Breast cancer is currently the second most common type of cancer amongst women. In 2001 over 190,000 new cases of invasive breast cancer and over 47, 000 additional cases of *in situ* breast cancer were diagnosed. Incidence and death rates increase with age, for the period 1994 - 1998 the incidence of breast cancer amongst women between the ages of 20 and 24 was only 1.5 per 100,000 population. However the risk increases to 489.7 within the age group 75 - 79. Mortality rates have decreased by approximately 5% over the last decade and factors affecting 5 year survival rates include age, stage of cancer, socioeconomic factors and race.

Breast cancer is defined as the uncontrolled proliferation of cells within breasts tissues. Breasts are comprised of 15 to 20 lobes joined together by ducts. Cancer arises most commonly in the duct, but is also found in the lobes with the rarest type of cancer termed inflammatory breast cancer.

It will be appreciated by those skilled in the art that there exists a continuing need to improve methods of early detection, classification and treatment of breast cancers. In contrast to the detection of some other common cancers such as cervical and dermal there are inherent difficulties in classifying and detecting breast cancers.

The first step of any treatment is the assessment of the patient's condition comparative to defined classifications of the disease. However the value of such a system is inherently dependant upon the quality of the classification. Breast cancers are staged according to their size, location and occurrence of metastasis. Methods of treatment include the use of surgery, radiation therapy, chemotherapy and endocrine therapy, which are also used as adjuvant therapies to surgery.

Endocrine therapies have been developed in order to block the effects of estrogen on cancer cells or to reduce serum estrogen levels. Tamoxifen (TAM) is the most widely used antioestrogenic drug for breast cancer patients. It acts blocking estrogen stimulation of breast cancer cells, inhibiting both translocation and nuclear binding of estrogen receptor. TAM is used in adjuvant setting for primary breast cancer patients and for the treatment of metastatic disease and its effectiveness has been proved in several clinical trials. Treatment for five years reduces annual disease recurrence by 47% and annual deaths by 26% and this reduction is similar in different age groups. Also it reduces the incidence of developing contralateral breast tumours. TAM is among the least toxic antineoplastic agents but as it has estrogenic properties in some tissues, it increases by 3 folds the risk of endometrial cancer. Other endocrine therapies include aromatase inhibitors, which block the enzyme aromatase in adipose tissue (the main source of estrogen in postmenopausal women) and lead to reduced or abolished production of estrogens in adipose tissue. Also, new agents which block or modulate the estrogen receptor have been developed, they are generally summarised as SERMs = selective estrogen receptor modulators. Yet another way to reduce the amount of estrogen available to the tumour is to apply agents which interrupt the feed-back loop in sex hormone regulation (LH-RH analogues) at a higher level.

In general, the side-effects of endocrine treatment are harmless compared to chemotherapy. However, as endocrine treatments eliminate or reduce estrogen as a growth factor for cancer, they work only for tumours which rely on estrogen as a growth factor. The growth of cancers which do not have a functional ER pathway cannot be modulated by endocrine therapies.

The current way to determine if a tumour will respond to endocrine therapies is the analysis of expression of hormone receptors. Hormone receptor status should be tested prior to any endocrine treatment as only a group of patients will benefit from therapy. For this purpose ER (estrogen receptor) and PR (progesterone receptor) status are tested routinely in all patients and they are considered predictive markers of response (a predictive marker or factor is any measurement associated with response or lack of response to a particular therapy). ER status is predictive of response in adjuvant endocrine therapy setting and also in advanced metastatic disease.

Currently, ER positive and or PR positive patients receive TAM and the remaining 10% of patients receive chemotherapy. The problem is that the endocrine treatment is only effective in a subgroup of hormone receptor positive patients and also, that a small subgroup of ER negative patients appear initially to respond to TAM. Then, the non responder subgroup will not only not benefit from endocrine treatment but have the adverse effects of it and will not have the opportunity to receive chemotherapy instead. On the other hand, the ER negative subgroup that could have benefit from endocrine treatment will receive instead chemotherapy. Several different assays are available to measure PR and ER, including biochemical and IHC (immunohistochemical) analysis, but there is a lack of standardisation of staining methods and interlaboratory variability (Clin Cancer Res 2000, 6:616-621).

Currently several predictive markers are under evaluation. As up to now most patients have received Tamoxifen as endocrine treatment most of the markers have been shown to be associated with response or resistance to tamoxifen. However, it is generally assumed that there is a large overlap between responders to one or the other endocrine treatment. In fact, ER and PR expression are used to select patients for any endocrine treatment. Among the markers which have been associated with TAM response is bcl-2. High bcl-2 levels showed promising correlation to TAM therapy response in patients with metastatic disease and prolonged survival and added valuable information to ER negative patient subgroup (J Clin Oncology 1997, 15 5:1916-1922; Endocrine, 2000, 13(1):1-10). There is conflicting evidence regarding the independent predictive value of c-erbB2 (Her2/neu) over expression in patients with advance breast cancer that require further evaluation and verification (British J of Cancer 1999, 79 (7/8):1220-1226; J Natl Cancer Inst, 1998,90 (21): 1601-1608).

Other predictive markers include SRC-1 (steroid receptor coactivator-1), CGA gene over expression, cell kinetics and S phase fraction assays (Breast Cancer Res and Treat, 1998, 48:87-92; Oncogene 2001, 20:6955-6959). Recently, uPA (Urokinase-type plasminogen activator) and PAI-1 (Plasminogen activator inhibitor type 1) together showed to be useful to define a subgroup of patients who have worse prognosis and who would benefit from adjuvant systemic therapy (J Clinical Oncology, 2002, 20 n° 4). All of these markers need further evaluations in prospective trials as none of them is yet a validated marker of response.

The gene stathimin (NM_005563) codes for an oncoprotein 18, also known as stathimin, a conserved cytosolic phosphoprotein that regulates microtubule dynamics. The protein is highly expressed in a variety of human malignancies. In human breast cancers the stahimin gene has shown to be up-regulated in a subset of the tumours.

The gene PITX-2 (NM_000325) encodes a transcription factor (PITX-2) which is known to be expressed during development of anterior structures such as the eye, teeth, and anterior pituitary. Although the expression of this gene is associated with cell differentiation and proliferation it has no heretofore recognised role in carcinogenesis or responsiveness to endocrine treatment. Furthermore, to date no known analysis of the methylation state of this gene has been published.

The gene PSA (Accession number NM_021154), is not to be confused with the gene also popularly referred to as PSA (Accession number NM_001648) which encodes prostate specific antigen and whose technically correct name is kallikrein 3. The gene PSA encodes the protein phosphoserine aminotransferase which is the second step-catalysing enzyme in the serine biosynthesis pathway Changes in gene expression levels have been monitored by mRNA expression analysis and upregulation of the gene has been identified in colonic carcinoma in a study of 6 samples (Electrophoresis 2002 Jun;23(11):1667-76 mRNA differential display of gene expression in colonic carcinoma. Ojala P, Sundstrom J, Gronroos JM, Virtanen E, Talvinen K, Nevalainen TJ.).

The gene CGA (Accession number NM_000735) encodes the alpha polypetptide of glycoprotein hormones. Further, it has been identified as an estrogen receptor alpha (ER alpha)-responsive gene and overexpression of the gene has been linked to ER positivity in breast tumours. Bieche et. al. examined mRNA levels of said gene in 125 ER alpha-positive

postmenopausal breast cancer patients treated with primary surgery followed by adjuvant tamoxifen therapy. Initial results indicated significant links between CGA gene overexpression and Scarff-Bloom-Richardson histopathological grade I+II and progesterone and estrogen receptor positivity, which suggested that CGA is a marker of low turnour aggressiveness ('Identification of CGA as a Novel Estrogen Receptor-responsive Gene in Breast Cancer: An Outstanding Candidate Marker to predict the Response to Endocrine Therapy Cancer Research' 61, 1652-1658, February 15, 2001. Ivan Bièche, Béatrice Parfait, Vivianne Le Doussal, Martine Olivi, Marie-Christine Rio, Rosette Lidereau and Michel Vidaud). Further mRNA expression analysis linked CGA expression levels to Tamoxifen response, it was postulated that when combined with analysis of the marker ERBB2 (a marker of poor response) the gene may be useful as a predictive marker of tamoxifen responsiveness in breast cancer (Oncogene 2001 Oct 18;20(47):6955-9 The CGA gene as new predictor of the response to endocrine therapy in ER alpha-positive postmenopausal breast cancer patients. Bieche I, Parfait B, Nogues C, Andrieu C, Vidaud D, Spyratos F, Lidereau R, Vidaud M.). The authors provided significant data associating the expression of the gene CGA with Endocrine treatment response. However, said analyses have all focused upon the analysis of relative levels of mRNA expression. This is not a methodology that is suitable for a medium or high throughput, nor is it a suitable basis for the development of a clinical assay.

Description

The present invention provides methods and nucleic acids for predicting the response of a patient with a cell proliferative disorder of the breast tissues to endocrine treatment. Using the methods and nucleic acids described herein, statistically significant models of patient responsiveness to said treatment regimen can be developed and utilised to assist patients and clinicians in determining treatment options. The described method is to be used to asses the suitability of endocrine treatment as a therapy for patients suffering from a cell proliferative disorder of the breast tissues. Thus, the present invention will be seen to reduce the problems associated with present treatment response prediction methods.

Using the methods and nucleic acids as described herein, patient responsiveness can be evaluated before or during endocrine treatment for a cell proliferative disorder of the breast tissues, in order to provide critical information to the patient and clinician as to the risks, burdens, and benefits associated endocrine treatment. It will be appreciated, therefore, that the

methods and nucleic acids exemplified herein can serve to improve a patient's quality of life and odds of treatment success by allowing both patient and clinician a more accurate assessment of the patient's treatment options.

The aim of the invention is achieved by means of the analysis of the methylation patterns of one or a combination of genes taken from the group PITX 2, PSA, CGA and STMN 1(see Table 1) and/or their regulatory regions. The invention is characterised in that the nucleic acid of one or a combination of genes taken from the group PITX 2, PSA, CGA and STMN 1 are contacted with a reagent or series of reagents capable of distinguishing between methylated and non methylated CpG dinucleotides within the genomic sequence of interest.

The present invention makes available a method for ascertaining genetic and/or epigenetic parameters of genomic DNA. The method is for use in the improved treatment and monitoring of breast cell proliferative disorders, by enabling the accurate prediction of a patient's response to endocrine treatment. In a particularly preferred embodiment, the method according to the invention enables the differentiation between patients who respond to endocrine therapy and those who do not.

The method according to the invention may be used for the analysis of a wide variety of cell proliferative disorders of the breast tissues including, but not limited to ductal carcinoma in situ, lobular carcinoma, colloid carcinoma, tubular carcinoma, medullary carcinoma, metaplastic carcinoma, intraductal carcinoma in situ, lobular carcinoma in situ and papillary carcinoma in situ.

The method according to the invention is particularly suited to the prediction of response to endocrine treatment in two treatment settings. In one embodiment, the method is applied to patients who receive endocrine treatment as secondary treatment to a primary treatment such as surgery (hereinafter referred to as the adjuvant setting) as illustrated in Figure 1. Such a treatment is often prescribed to patients suffering from Stage 1 to 3 breast carcinomas. In this embodiment responders are defined as those who do not have a detectable relapse of the breast cancer in a specified period of time, non responders are those who relapse within said time period. In this embodiment it is preferred that the target nucleic acids are of the gene PITX 2 and/or its regulatory regions. In this embodiment of the method it is preferred that the

method according to the invention is applied only to patients who are estrogen and/or progesterone receptor marker positive.

In a further embodiment said method is applied to patients suffering from a relapse of breast cancer following treatment by a primary means (preferably surgery) followed by a disease free period, and wherein the endocrine treatment has been prescribed in response to a detection of a relapse of the carcinoma. Such a treatment is often prescribed to patients suffering from later stage carcinomas, particularly wherein metastasis has occurred. Therefore this clinical setting shall also hereinafter be referred to as the 'metastatic setting'. In this embodiment it is preferred that the target nucleic acids are derived from one or more of the genes taken from the group PSA, CGA and STMN 1 and/or their regulatory regions. In this embodiment responders are those who enter partial or complete remission i.e. subjects whose cancer recedes to undetectable levels as opposed to those whose diseases further metastasise or remain above detectable levels. This methodology present further improvements over the state of the art in that the method may be applied to any subject, independent of the estrogen and/or progesterone receptor status. Therefore in a preferred embodiment, the subject is not required to have been tested for estrogen or progesterone receptor status. In one embodiment of the method the methodology is applied to subjects who have not received chemotherapy, wherein said genes are selected from the group comprising PSA, CGA, and STMN 1. Furthermore, wherein said patients have been treated with chemotherapy said group of genes need not include the gene STMN 1.

Furthermore, the method enables the analysis of cytosine methylations and single nucleotide polymorphisms within said genes.

The object of the invention is achieved by means of the analysis of the methylation patterns of the genes PITX 2, PSA, CGA, and STMN 1 and/or their regulatory regions, in a particularly preferred embodiment the sequences comprising SEQ ID Nos: 27, 90, 91 and 83 and sequences complementary thereto. In a preferred embodiment said method is achieved by contacting said nucleic acid sequences in a biological sample obtained from a subject with at least one reagent or a series of reagents, wherein said reagent or series of reagents, distinguishes between methylated and non methylated CpG dinucleotides within the target nucleic acid.

In a preferred embodiment, the method comprises the following steps:

In the first step of the method the genomic DNA sample must be isolated from sources such as cells or cellular components which contain DNA, sources of DNA comprising, for example, cell lines, histological slides, biopsies, tissue embedded in paraffin, breast tissues, blood, plasma, lymphatic fluid, lymphatic tissue, duct cells, ductal lavage fluid, nipple aspiration fluid, bone marrow and combinations thereof. Extraction may be by means that are standard to one skilled in the art, these include the use of detergent lysates, sonification and vortexing with glass beads. Once the nucleic acids have been extracted the genomic double stranded DNA is used in the analysis.

In a preferred embodiment the DNA may be cleaved prior to the next step of the method, this may be by any means standard in the state of the art, in particular, but not limited to, with restriction endonucleases.

In the second step of the method, the genomic DNA sample is treated in such a manner that cytosine bases which are unmethylated at the 5'-position are converted to uracil, thymine, or another base which is dissimilar to cytosine in terms of hybridisation behaviour. This will be understood as 'pretreatment' hereinafter.

The above described treatment of genomic DNA is preferably carried out with bisulfite (sulfite, disulfite) and subsequent alkaline hydrolysis which results in a conversion of non-methylated cytosine nucleobases to uracil or to another base which is dissimilar to cytosine in terms of base pairing behaviour. If bisulfite solution is used for the reaction, then an addition takes place at the non-methylated cytosine bases. Moreover, a denaturating reagent or solvent as well as a radical interceptor must be present. A subsequent alkaline hydrolysis then gives rise to the conversion of non-methylated cytosine nucleobases to uracil. The converted DNA is then used for the detection of methylated cytosines.

Fragments of the pretreated DNA are amplified, using sets of primer oligonucleotides, and a preferably heat-stable, polymerase. Because of statistical and practical considerations, preferably more than ten different fragments having a length of 100 - 2000 base pairs are amplified. The amplification of several DNA segments can be carried out simultaneously in one and the same reaction vessel. Usually, the amplification is carried out by means of a polymerase chain reaction (PCR).

The design of such primers is obvious to one skilled in the art. These should include at least two oligonucleotides whose sequences are each reverse complementary or identical to an at least 18 base-pair long segment of the following base sequences specified in the appendix: SEQ ID NO 188, 189, 430, 431, 314-317, 556-559, 300, 301, 542 and 543. Said primer oligonucleotides are preferably characterised in that they do not contain any CpG dinucleotides. In a particularly preferred embodiment of the method, the sequence of said primer oligonucleotides are designed so as to selectively anneal to and amplify, only the breast cell specific DNA of interest, thereby minimising the amplification of background or non relevant DNA. In the context of the present invention, background DNA is taken to mean genomic DNA which does not have a relevant tissue specific methylation pattern, in this case, the relevant tissue being breast tissues.

According to the present invention, it is preferred that at least one primer oligonucleotide is bound to a solid phase during amplification. The different oligonucleotide and/or PNA-oligomer sequences can be arranged on a plane solid phase in the form of a rectangular or hexagonal lattice, the solid phase surface preferably being composed of silicon, glass, polystyrene, aluminium, steel, iron, copper, nickel, silver, or gold, it being possible for other materials such as nitrocellulose or plastics to be used as well.

The fragments obtained by means of the amplification may carry a directly or indirectly detectable label. Preferred are labels in the form of fluorescence labels, radionuclides, or detachable molecule fragments having a typical mass which can be detected in a mass spectrometer, it being preferred that the fragments that are produced have a single positive or negative net charge for better detectability in the mass spectrometer. The detection may be carried out and visualised by means of matrix assisted laser desorption/ionisation mass spectrometry (MALDI) or using electron spray mass spectrometry (ESI).

In the next step the nucleic acid amplificates are analysed in order to determine the methylation status of the genomic DNA prior to treatment.

The post treatment analysis of the nucleic acids may be carried out using alternative methods. Several methods for the methylation status specific analysis of the treated nucleic acids are described below, other alternative methods will be obvious to one skilled in the art.

Using several methods known in the art the analysis may be carried out during the amplification step of the method. In one such embodiment, the methylation status of preselected CpG positions within the genes PITX 2, PSA, CGA, and STMN 1 and/or their regulatory regions may be detected by use of methylation specific primer oligonucleotides. This technique has been described in U.S. Patent 6,265,171 to Herman. The use of methylation status specific primers for the amplification of bisulphite treated DNA allows the differentiation between methylated and unmethylated nucleic acids. MSP primers pairs contain at least one primer which hybridises to a bisulphite treated CpG dinucleotide. Therefore the sequence of said primers comprises at least one CG, TG or CA dinucleotide. MSP primers specific for non methylated DNA contain a 'T' at the 3' position of the C position in the CpG. According to the present invention, it is therefore preferred that the base sequence of said primers is required to comprise a sequence having a length of at least 9 nucleotides which hybridises to a pretreated nucleic acid sequence according to SEQ ID Nos 188, 189, 430, 431, 314-317, 556-559, 300, 301, 542 and 543 and sequences complementary thereto wherein the base sequence of said oligomers comprises at least one CG, TG or CA dinucleotide.

In one embodiment of the method the methylation status of the CpG positions may be determined by means of hybridisation analysis. In this embodiment of the method the amplificates obtained in the second step of the method are hybridised to an array or a set of oligonucleotides and/or PNA probes. In this context, the hybridisation takes place in the manner described as follows. The set of probes used during the hybridisation is preferably composed of at least 4 oligonucleotides or PNA-oligomers. In the process, the amplificates serve as probes which hybridise to oligonucleotides previously bonded to a solid phase. The non-hybridised fragments are subsequently removed. Said oligonucleotides contain at least one base sequence having a length of 10 nucleotides which is reverse complementary or identical to a segment of the base sequences specified in the appendix, the segment containing at least one CpG or TpG dinucleotide. In a further preferred embodiment the cytosine of the CpG dinucleotide, or in the case of TpG, the thiamine, is the 5th to 9th nucleotide from the 5'-end of the 10-mer. One oligonucleotide exists for each CpG or TpG dinucleotide.

The non-hybridised amplificates are then removed. In the final step of the method, the hybridised amplificates are detected. In this context, it is preferred that labels attached to the

amplificates are identifiable at each position of the solid phase at which an oligonucleotide sequence is located.

In a further embodiment of the method the methylation status of the CpG positions may be determined by means of oligonucleotide probes that are hybridised to the treated DNA concurrently with the PCR amplification primers (wherein said primers may either be methylation specific or standard).

A particularly preferred embodiment of this method is the use of fluorescence-based Real Time Quantitative PCR (Heid et al., Genome Res. 6:986-994, 1996) employing a duallabelled fluorescent oligonucleotide probe (TaqMan™ PCR, using an ABI Prism 7700 Sequence Detection System, Perkin Elmer Applied Biosystems, Foster City, California). The TaqMan™ PCR reaction employs the use of a nonextendible interrogating oligonucleotide, called a TaqMan[™] probe, which is designed to hybridise to a GpC-rich sequence located between the forward and reverse amplification primers. The TaqManTM probe further comprises a fluorescent "reporter moiety" and a "quencher moiety" covalently bound to linker moieties (e.g., phosphoramidites) attached to the nucleotides of the $TaqMan^{TM}$ oligonucleotide. For analysis of methylation within nucleic acids subsequent to bisulphite treatment it is required that the probe be methylation specific, as described in U.S. 6,331,393, (hereby incorporated by reference) also known as the Methyl Light assay. Variations on the TaqMan[™] detection methodology that are also suitable for use with the described invention include the use of dual probe technology (LightcyclerTM) or fluorescent amplification primers (SunriseTM technology). Both these techniques may be adapted in a manner suitable for use with bisulphite treated DNA, and moreover for methylation analysis within CpG dinucleotides.

A further suitable method for the use of probe oligonucleotides for the assessment of methylation by analysis of bisulphite treated nucleic acids is the use of blocker oligonucleotides. The use of such oligonucleotides has been described in BioTechniques 23(4), 1997, 714-720 D. Yu, M.Mukai, Q. Liu, C. Steinman. Blocking probe oligonucleotides are hybridised to the bisulphite treated nucleic acid concurrently with the PCR primers. PCR amplification of the nucleic acid is terminated at the 5' position of the blocking probe, thereby amplification of a nucleic acid is suppressed wherein the complementary sequence to the blocking probe is present. The probes may be designed to hybridise to the bisulphite treated

nucleic acid in a methylation status specific manner. For example, for detection of methylated nucleic acids within a population of unmethylated nucleic acids suppression of the amplification of nucleic acids which are unmethylated at the position in question would be carried out by the use of blocking probes comprising a 'CG' at the position in question, as opposed to a 'CA'.

In a further preferred embodiment of the method the determination of the methylation status of the CpG positions is carried out by the use of template directed oligonucleotide extension, such as MS SNuPE as described by Gonzalgo and Jones (Nucleic Acids Res. 25:2529-2531).

In a further embodiment of the method the determination of the methylation status of the CpG positions is enabled by sequencing and subsequent sequence analysis of the amplificate generated in the second step of the method (Sanger F., et al., 1977 PNAS USA 74: 5463-5467).

A further embodiment of the invention is a method for the analysis of the methylation status of genomic DNA without the need for pretreatment. In the first and second steps of the method the genomic DNA sample must be obtained and isolated from tissue or cellular sources. Such sources may include cell lines, histological slides, body fluids, or tissue embedded in paraffin. Extraction may be by means that are standard to one skilled in the art, these include the use of detergent lysates, sonification and vortexing with glass beads. Once the nucleic acids have been extracted the genomic double stranded DNA is used in the analysis.

In a preferred embodiment the DNA may be cleaved prior to the treatment, this may be by any means standard in the state of the art, in particular with restriction endonucleases. In the third step, the DNA is then digested with one or more methylation sensitive restriction enzymes. The digestion is carried out such that hydrolysis of the DNA at the restriction site is informative of the methylation status of a specific CpG dinucleotide.

In a preferred embodiment the restriction fragments are amplified. In a further preferred embodiment this is carried out using the polymerase chain reaction.

In the final step the amplificates are detected. The detection may be by any means standard in the art, for example, but not limited to, gel electrophoresis analysis, hybridisation analysis, incorporation of detectable tags within the PCR products, DNA array analysis, MALDI or ESI analysis.

The aforementioned method is preferably used for ascertaining genetic and/or epigenetic parameters of genomic DNA.

In order to enable this method, the invention further provides the modified DNA of one or a combination of genes taken from the group PITX 2, PSA, CGA, and STMN 1 as well as oligonucleotides and/or PNA-oligomers for detecting cytosine methylations within said genes. The present invention is based on the discovery that genetic and epigenetic parameters and, in particular, the cytosine methylation patterns of said genomic DNAs are particularly suitable for improved treatment and monitoring of breast cell proliferative disorders.

The nucleic acids according to the present invention can be used for the analysis of genetic and/or epigenetic parameters of genomic DNA.

This objective according to the present invention is achieved using a nucleic acid containing a sequence of at least 18 bases in length of the pretreated genomic DNA according to one of SEQ ID NO 188, 189, 430, 431, 314-317, 556-559, 300, 301, 542, and 543 and sequences complementary thereto.

The modified nucleic acids could heretofore not be connected with the ascertainment of disease relevant genetic and epigenetic parameters.

The object of the present invention is further achieved by an oligonucleotide or oligomer for the analysis of pretreated DNA, for detecting the genomic cytosine methylation state, said oligonucleotide containing at least one base sequence having a length of at least 10 nucleotides which hybridises to a pretreated genomic DNA according to SEQ ID NO 188, 189, 430, 431, 314-317, 556-559, 300, 301, 542, and 543. The oligomer probes according to the present invention constitute important and effective tools which, for the first time, make it possible to ascertain specific genetic and epigenetic parameters during the analysis of biological samples for features associated with a patient's response to endocrine treatment.

Said oligonucleotides allow the improved treatment and monitoring of breast cell proliferative disorders. The base sequence of the oligomers preferably contains at least one CpG or TpG dinucleotide. The probes may also exist in the form of a PNA (peptide nucleic acid) which has particularly preferred pairing properties. Particularly preferred are oligonucleotides according to the present invention in which the cytosine of the CpG dinucleotide is within the middle third of said oligonucleotide e.g. the 5th - 9th nucleotide from the 5'-end of a 13-mer oligonucleotide; or in the case of PNA-oligomers, it is preferred for the cytosine of the CpG dinucleotide to be the 4th - 6th nucleotide from the 5'-end of the 9-mer.

The oligomers according to the present invention are normally used in so called "sets" which contain at least one oligomer for each of the CpG dinucleotides within SEQ ID NO 188, 189, 430, 431, 314-317, 556-559, 300, 301, 542 and 543.

In a particularly preferred embodiment of the method the oligomers according to SEQ ID NOs: 1816, 1816, 1817, 1817, 1818, 1818, 1819, 1819, 1820, 1820, 1821, 1821, 1822, 1822, 1823, 1823 - 1838, 1838, 1839, 1839, 1840, 1840, 1841, 1841, 1842, 1842, 1843, 1843 are used for predicting a subject's response to endocrine treatment in an adjuvant setting. In a further particularly preferred embodiment of the method the oligomers according to SEQ ID NOs: 1816, 1816, 1817, 1817, 1818, 1818, 1819, 1819, 1820, 1820, 1821, 1821, 1822, 1822, 1823, 1823 to 1837 are used for predicting a subject's response to endocrine treatment in an metastatic setting.

In the case of the sets of oligonucleotides according to the present invention, it is preferred that at least one oligonucleotide is bound to a solid phase. It is further preferred that all the oligonucleotides of one set are bound to a solid phase.

The present invention further relates to a set of at least 10 n (oligonucleotides and/or PNA-oligomers) used for detecting the cytosine methylation state of genomic DNA, by analysis of said sequence or treated versions of said sequence (of the genes PITX 2, PSA, CGA, and STMN 1, as detailed in the sequence listing and Table 1) and sequences complementary thereto). These probes enable improved treatment and monitoring of breast cell proliferative disorders.

The set of oligomers may also be used for detecting single nucleotide polymorphisms (SNPs) by analysis of said sequence or treated versions of said sequence (of the genes PITX 2, PSA, CGA, and STMN 1, as detailed in the sequence listing and Table 1).

It will be obvious to one skilled in the art that the method according to the invention will be improved and supplemented by the incorporation of markers and clinical indicators known in the state of the art and currently used as predictive of the outcome Endocrine treatment. More preferably said markers include node status, age, menopausal status, grade, estrogen and progesterone receptors.

The genes that form the basis of the present invention may also be used to form a "gene panel", i.e. a collection comprising the particular genetic sequences of the present invention and/or their respective informative methylation sites. The formation of gene panels allows for a quick and specific analysis of specific aspects of breast cancer treatment. The gene panel(s) as described and employed in this invention can be used with surprisingly high efficiency for the treatment of breast cell proliferative disorders by prediction of the outcome of treatment with the drug Tamoxifen.

The efficiency of the method according to the invention is improved when applied to patients who have not been treated with chemotherapy. Accordingly, it is a particularly preferred embodiment of the method wherein the method is used for the assessment of subjects who have not undergone chemotherapy.

In addition, the use of multiple CpG sites from a diverse array of genes allows for a relatively high degree of sensitivity and specificity in comparison to single gene prognostic tools.

According to the present invention, it is preferred that an arrangement of different oligonucleotides and/or PNA-oligomers (a so-called "array") made available by the present invention is present in a manner that it is likewise bound to a solid phase. This array of different oligonucleotide- and/or PNA-oligomer sequences can be characterised in that it is arranged on the solid phase in the form of a rectangular or hexagonal lattice. The solid phase surface is preferably composed of silicon, glass, polystyrene, aluminium, steel, iron, copper, nickel, silver, or gold. However, nitrocellulose as well as plastics such as nylon which can exist in the form of pellets or also as resin matrices are suitable alternatives.

Therefore, a further subject matter of the present invention is a method for manufacturing an array fixed to a carrier material for the improved treatment and monitoring of breast cell proliferative disorders. In said method at least one oligomer according to the present invention is coupled to a solid phase. Methods for manufacturing such arrays are known, for example, from US Patent 5,744,305 by means of solid-phase chemistry and photolabile protecting groups.

A further subject matter of the present invention relates to a DNA chip for the improved treatment and monitoring of breast cell proliferative disorders. The DNA chip contains at least one nucleic acid according to the present invention. DNA chips are known, for example, in US Patent 5,837,832.

Moreover, a subject matter of the present invention is a kit which may be composed, for example, of a bisulfite-containing reagent, a set of primer oligonucleotides containing at least two oligonucleotides whose sequences in each case correspond to or are complementary to a 18 base long segment of the base sequences specified in SEQ ID NOs: 188, 189, 430, 431, 314 to 317, 556-559, 300, 301, 542, and 543, oligonucleotides and/or PNA-oligomers as well as instructions for carrying out and evaluating the described method.

In a further preferred embodiment said kit may further comprise standard reagents for performing a CpG position specific methylation analysis wherein said analysis comprises one or more of the following techniques: MS-SNuPE, MSP, Methyl light, Heavy Methyl, and nucleic acid sequencing. However, a kit along the lines of the present invention can also contain only part of the aforementioned components.

The oligomers according to the present invention or arrays thereof as well as a kit according to the present invention are intended to be used for the improved treatment and monitoring of breast cell proliferative disorders. According to the present invention, the method is preferably used for the analysis of important genetic and/or epigenetic parameters within genomic DNA, in particular for use in improved treatment and monitoring of breast cell proliferative disorders.

The methods according to the present invention are used, for improved treatment and monitoring of breast cell proliferative disorder by enabling more informed treatment regimens.

The present invention moreover relates to the diagnosis and/or prognosis of events which are disadvantageous or relevant to patients or individuals in which important genetic and/or epigenetic parameters within genomic DNA, said parameters obtained by means of the present invention may be compared to another set of genetic and/or epigenetic parameters, the differences serving as the basis for the diagnosis and/or prognosis of events which are disadvantageous or relevant to patients or individuals. Examples of such parameters include, but are not limited to the assessment of estrogen and progesterone markers.

In the context of the present invention the term "hybridisation" is to be understood as a bond of an oligonucleotide to a completely complementary sequence along the lines of the Watson-Crick base pairings in the sample DNA, forming a duplex structure.

In the context of the present invention, "genetic parameters" are mutations and polymorphisms of genomic DNA and sequences further required for their regulation. To be designated as mutations are, in particular, insertions, deletions, point mutations, inversions and polymorphisms and, particularly preferred, SNPs (single nucleotide polymorphisms).

In the context of the present invention the term "methylation state" is taken to mean the degree of methylation present in a nucleic acid of interest, this may be expressed in absolute or relative terms i.e. as a percentage or other numerical value or by comparison to another tissue and therein described as hypermethylated, hypomethylated or as having significantly similar or identical methylation status.

In the context of the present invention the term "regulatory region" of a gene is taken to mean nucleotide sequences which affect the expression of a gene. Said regulatory regions may be located within, proximal or distal to said gene. Said regulatory regions include but are not limited to constitutive promoters, tissue-specific promoters, developmental-specific promoters, inducible promoters and the like. Promoter regulatory elements may also include certain enhancer sequence elements that control transcriptional or translational efficiency of the gene.

In the context of the present invention the term "chemotherapy" is taken to mean the use of drugs or chemical substances to treat cancer. This definition excludes radiation therapy (treatment with high energy rays or particles), hormone therapy (treatment with hormones or hormone analogues (synthetic substitutes) and surgical treatment.

In the context of the present invention, "epigenetic parameters" are, in particular, cytosine methylations and further modifications of DNA bases of genomic DNA and sequences further required for their regulation. Further epigenetic parameters include, for example, the acetylation of histones which, cannot be directly analysed using the described method but which, in turn, correlates with the DNA methylation.

In the context of the present invention the term "adjuvant treatment" is taken to mean a therapy of a cancer patient immediately following an initial non chemotherapeutical therapy, e.g. surgery. In the context of the present invention, said adjuvant treatment is performed using Tamoxifen. In general, the purpose of an adjuvant therapy is to provide a significantly smaller risk of recurrences compared without the adjuvant therapy.

In the context of the present invention the term "estrogen and/or progesterone receptor positive" is taken to mean cells that expresses on its surface receptors that are susceptible to the binding of estrogens and/or progesterones.

In the following, the present invention will be explained in greater detail on the basis of the sequences, figures and examples without being limited thereto.

Figure 1 shows a preferred application of the method according to the invention. The X axis shows the tumour(s) mass, wherein the line '3' shows the limit of detectability. The Y-axis shows time. Accordingly said figure illustrates a simplified model of endocrine treatment of an Stage 1-3 breast tumour wherein primary treatment was surgery (at point 1), followed by adjuvant therapy with Tamoxifen. In a first scenario a responder to treatment (4) is shown as remaining below the limit of detectability for the duration of the observation. A non responder to the treatment (5) has a period of disease free survival (2) followed by relapse when the carcinoma mass reaches the level of detectability.

Figure 2 shows another preferred application of the method according to the invention. The X axis shows the tumour(s) mass, wherein the line '3' shows the limit of detectability. The Y-axis shows time. Accordingly said figure illustrates a simplified model of Endocrine treatment of an late stage breast tumour wherein primary treatment was surgery (at point 1), followed by relapse which is treated by Tamoxifen (2). In a first scenario a responder to treatment (4) is shown as remaining below the limit of detectability for the duration of the observation. A non responder to the treatment (5) does not recover from the relapse.

Figures 3 and 4 show a ranked matrix of data obtained according to Example 3 according to CpG methylation differences between the two classes of tissues (responder and non-responder to endocrine treatment in a metastatic setting), using an algorithm. The Figures are shown in greyscale, wherein the most significant CpG positions are at the bottom of the matrix with significance decreasing towards the top. Black indicates total methylation at a given CpG position, white represents no methylation at the particular position, with degrees of methylation represented in grey, from light (low proportion of methylation) to dark (high proportion of methylation). Each row represents one specific CpG position within a gene and each column shows the methylation profile for the different CpGs for one sample. On the left side a CpG and gene identifier is shown this may be cross referenced with the accompanying table (Table 3) in order to ascertain the gene in question and the detection oligomer used. On the right side p values for the individual CpG positions are shown. The p values are the probabilities that the observed distribution occurred by chance in the data set.

SEQ ID Nos: 1 to 121 represent 5' and/or regulatory regions and/or CpG rich regions of the genes according to Table 1. These sequences are derived from Genbank and will be taken to include all minor variations of the sequence material which are currently unforeseen, for example, but not limited to, minor deletions and SNPs.

SEQ ID Nos: 136 to 619 exhibit the pretreated sequence of DNA derived from the genomic sequence according to Table 1. These sequences will be taken to include all minor variations of the sequence material which are currently unforeseen, for example, but not limited to, minor deletions and SNPs.

SEQ ID Nos: 122 to 135 exhibit the sequence of oligomers which are useful for the analysis of CpG positions within genomic DNA according to SEQ ID Nos: 1 to 121 according to Tables 2 and 3.

SEQ ID NO: 856 to SEQ ID NO: 1843 exhibit the sequence of oligomers which are particularly useful for the analysis of pretreated DNA according to SEQ ID NO: 136 to SEQ ID NO: 619.

Examples

In the following examples, multiplex PCR of genes according to Table 1 was carried out on tissue samples from breast cancer patients treated with the drug Tamoxifen. Two sets of tissues were acquired, in the first set patients received Tamoxifen treatment upon detection of a relapse of breast cancer following surgical treatment (hereinafter referred to as the 'metastatic' setting), wherein breast cancer receded to non detectable levels the patient was termed a 'responder', wherein the cancer remained at detectable levels the patient was termed a non-responder. In the second set of samples, patients were treated with Tamoxifen subsequent to surgery and wherein a relapse (detection of breast cancer) occurred the patients were termed 'non-responders', wherein no relapse was detected patients were termed 'responders'. Comparisons of the methylation profiles of responders to the drug to non responders to the drug in both the adjuvant and metastatic settings (See figures 1 and 2) was carried out as follows.

Each sample was treated in the manner described below in Example 1 in order to deduce the methylation status of CpG positions. The CpG methylation information for each sample was collated and then used in an analysis, as detailed in Example 2 (Metastatic setting) and Example 3 (Adjuvant setting).

Example 1

In the first step the genomic DNA was isolated from the cell samples using the Wizzard kit (Promega).

The isolated genomic DNA from the samples are treated using a bisulfite solution (hydrogen sulfite, disulfite). The treatment is such that all non methylated cytosines within the sample

are converted to thiamidine, conversely 5-methylated cytosines within the sample remain unmodified.

The treated nucleic acids were then amplified using multiplex PCRs, amplifying 8 fragments per reaction with Cy5 fluorescently labelled primers. PCR primers used are described in Table 2. PCR conditions were as follows.

Reaction solution:

10 ng bisulfite treated DNA

3,5 mM MgCl₂

400 μM dNTPs

2 pmol each primer

1 U Hot Star Taq (Qiagen)

Forty cycles were carried out as follows. Denaturation at 95°C for 15 min, followed by annealing at 55°C for 45 sec., primer elongation at 65°C for 2 min. A final elongation at 65°C was carried out for 10 min.

All PCR products from each individual sample were then hybridised to glass slides carrying a pair of immobilised oligonucleotides for each CpG position under analysis. Each of these detection oligonucleotides was designed to hybridise to the bisulphite converted sequence around one CpG site which was either originally unmethylated (TG) or methylated (CG). See Table 2 for further details of all hybridisation oligonucleotides used. Hybridisation conditions were selected to allow the detection of the single nucleotide differences between the TG and CG variants.

5 μ l volume of each multiplex PCR product was diluted in 10 x Ssarc buffer (10 x Ssarc:230 ml 20 x SSC, 180 ml sodium lauroyl sarcosinate solution 20%, dilute to 1000 ml with dH₂O). The reaction mixture was then hybridised to the detection oligonucleotides as follows. Denaturation at 95°C, cooling down to 10°C, hybridisation at 42°C overnight followed by washing with 10 x Ssarc and dH₂O at 42°C.

Fluorescent signals from each hybridised oligonucleotide were detected using genepix scanner and software. Ratios for the two signals (from the CG oligonucleotide and the TG

oligonucleotide used to analyse each CpG position) were calculated based on comparison of intensity of the fluorescent signals.

Example 2: Metastatic setting

The data obtained according to Example 1 is then sorted into a ranked matrix (as shown in Figures 3 and 4) according to CpG methylation differences between the two classes of tissues, using an algorithm. The most significant CpG positions are at the bottom of the matrix with significance decreasing towards the top. Black indicates total methylation at a given CpG position, white represents no methylation at the particular position, with degrees of methylation represented in grey, from light (low proportion of methylation) to dark (high proportion of methylation). Each row represents one specific CpG position within a gene and each column shows the methylation profile for the different CpGs for one sample. On the left side a CpG and gene identifier is shown this may be cross referenced with the accompanying table (Table 2) in order to ascertain the gene in question and the detection oligomer used. On the right side p values for the individual CpG positions are shown. The p values are the probabilities that the observed distribution occurred by chance in the data set.

Figure 3 shows the analysis of the total sample set wherein responders to the drug and compared to non responders, significant differences in methylation between the two classes of tissue were observed in the genes STMN 1 and PSA.

Wherein patients who had received chemotherapy as an additional therapy were excluded from the data set, an additional marker was observed CGA (see Figure 4).

Example 3: Adjuvant setting

Every CpG was put into a Cox proportional hazard model together with the known predictive markers N-stage and tumour size. The best marker was the gene PITX 2.

The Cox model for the best marker (oligonucleotide number 3522:2087) is:

	coef	Exp(coef)	Se(coef)	z	P ;
nStage	1.677	5.35	0.5390	3.11	0.00190

3522:2087	2.885	17.90	10.00		
	2.005	17.90	0.8211	3.51	0.00044
Tumour Size	0.120	1.13	0.0926	1.30	
			1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	1.50	0.19000

This shows that 3522:2087 gives information about survival time independent of nStage. The tumour size has no significant predictive power for expected survival time.

Table 1: Genes amplified according to Example 1.

No:	Gene:	Primer:	Amplificate
İ	ABCB1 (SEQ ID	TAAGTATGTTGAAGAAAGATTATTGT	Length:
•	NO: 1)	AG (SEQ ID NO: 620)	033
<i>,</i>	' '' .	TAAAACTATCCCATAATAACTCCCA	
	• •	AC (SEQ ID NO: 621)	
2	APOC2 (SEQ ID	ATGAGTAGAAGAGGTGATHE	
•	NO: 2)		533
٠. ٠ ٠		NO: 622) CCCTAAATCCCTTTCTTACC (SEQ ID NO: 623)	
,	CACNAIG (SEO	GGGATTTA A GA	,
	ID NO: 3)	GGGATTTAAGAGAAATTGAGGTA	707
	110.3)	(SEQ ID NO: 624)	, ,
;		AAACCCCAAACATCCTTTAT (SEQ ID	, .
<u> </u>	ECD4 (CDC TD	_INO: 023)	
٠,	EGR4 (SEQ ID	AGGGGGATTGAGTGTTAAGT (SEQ ID.	293
	NO: 4)	PNO: 027) CCCAAACATAAACACA A A A T	
		(OEO ID NO: 676)	1
	AR (SEQ ID NO:	GTAGTAGTAGTAAGAGA (SEQ ID	160
	5)	NO: 628) ACCCCCTAAATAATTATCCT	7100
	-1	(SEQ ID NO: 629)	
	RB1 (SEQ ID	TTTAACTTTCTTCTTCTTCT	710
	NO: 6)	ID NO: 630)	718
		TCCTACTCTAAATCCTCCTCAA (SEQ	
		ID NO: 631)	
	GP1BB (SEQ ID	GGTGATACCACAATT	
, ,	NO: 7)	GGTGATAGGAGAATAATGTTGG (SEQ ID NO: 632)	379 :
		TCTCCCA A CTA CA A CTA	
	. ,	TCTCCCAACTACAACCAAAC (SEQ ID	. ,
 -	WT1 (CEO'ID	INO: 033)	•
	WT1 (SEQ ID NO: 8)	AAAGGGAAATTAAGTGTTGT (SEQ ID	747
	μνο: 8)	INO: 033) IAACTACCCTCAACTTCCC	
	TYT A TO COTTO	(SEQ ID NO: 634)	,
	HLA-F (SEQ ID	TTGTTGTTTTAGGGGTTTTGG (SEQ	946
	NO: 9)	ן אט (1950 : 1970 עון	
		TCCTTCCCATTCTCCAAATATC (SEQ	••
		ID NO: 637)	•
)	ELK1 (SEQ ID	A A CTCTTTLA CTTTTT	200
ĺ	NO: 10)	(SEQ ID NO: 638)	966 .
	-	CAAACCCAAAACTCACCTAT (SEQ ID	
	•	NO: 639)	•
	ARHI (SEQ ID	GTGAGTTTTTCCCCCTCTTTT	
- 1		NO: 640)	142

•

•		TCAATCTTACTTTCACACTACATAA	1
		_(SEQ ID NO: 641)	
[2	BCL2 (SEQ ID	GTATTTTATGTTAAGGGGGAAA (SEQ	(40:
	NO: 13)	ID NO: 642) AAAAACCACAATCCTCCC	640
		(SEQ ID NO: 643)	
13	BRCA1 (SEQ ID	TCCATCOCA ATTOCATION	
	NO: 14)		537 .
	INO: 14)	INO: 644) TTAACCACCCAATCTACCC	
		(SEO ID NO: 645)	
14	CALCA (SEQ ID	GTTTTCC A A OTTATION A COLOR	C1 4
	NO: 15)	NO: 646)	614
•			·
		CCAAATTCTAAACCAATTTCC (SEQ ID NO: 647)	
5	CCNIDO (CEO ID		1
	CCND2 (SEQ ID		426
	NO: 16)	NO: 648) CCTAACCTCCTTCCTTTAACT	
<u>-</u>		(SEQ ID NO: 649)	
6	CDH1 (SEQ ID	GA CCTTCCCCCTTT + C + C +	
	NO: 17)	NO: 650)	478
	1.	CAAACTCACAAATACTTTACAATTC	
7	CDIDIO	(SEQ ID NO: 651)	
7.	CDKN1B (SEQ	GTGGGGAGGTÁGTTGAAGA (SEQ ID	478
	ID NO: 18)	NO: 652) ATACACCCTAACCCAAAAT	7 / 9
		(SEQ ID NO: 653)	
8	CDKN2A (SEQ	TTGAAAATTAAGGGTT	·
	ID NO: 19)	TTGAAAATTAAGGGTTGAGG (SEQ ID	598
	10 140. 19)	PIO: 034) CACCUTCTAATAACCAACCA	
	CD 750 70 1	(SEQ ID NO: 655)	
9	CDKN2A (SEQ	GGGGTTGGTTATTAGA (SEQ ID	256
•	ID NO: 19)	NO: 656) AACCCTCTACCCACCTAAAT	
		(SEQ ID NO: 657)	•
0	CDKN2B (SEQ	GGTTGGTTCA A COA + TO A	
	ID NO: 20)	GGTTGGTTGAAGGAATAGAAAT (SEQ	708
•	110. 20)	ן אַרַס : אַן בֿען (אַכּס : טאַן בען	
• •		CCCACTAAACATACCCTTATTC (SEQ	
<u>,':</u>		ДD NO: 659)	
1	CD44 (SEQ ID	GAAAGGAGAGGTTAAAGGTTG (SEQ	COC
•	NO: 21)	ID NO: 660)	096 .
•		AACTCACTTAACTCCAATCC	• • • • • • • • • • • • • • • • • • • •
		AACTCACTTAACTCCAATCCC (SEQ ID NO: 661)	•
2			
-	CSPG2 (SEQ ID	GGATAGGAGTTGGGATTAAGAT (SEQ	114
	10.22)	μD NO: 062)	· = •
•	1	AAATCTTTTTCAACACCAAAAT (SEQ	•
,		ID NO: 663)	•
3	DAPK1 (SEO ID	A A C C C T T T C T T C A A A T T T C T T	
	NO: 23)	ID NO: 664)	348
. •		TC A TTC C C C C C C C C C C C C C C C C	
		TGATTGGGTTTTAGGGAAATA (SEQ ID	
		NO: 003)	•
1	GGT1 (SEQ ID	GTGAAGGGTGTGAGTTGTTTA (SEQ IDS	62
	NO: 24)	NO: 666) CACAATCAATTTCCCACAA	002 ,
		(SEO ID NO. 667)	
;	GSTP1 (SEQ ID	(SEQ ID NO: 667)	
		ATTTGGGAAAGAGGGAAAG (SEQ ID 3	00
	F 10. 23)	NO: 668) TAAAAACTCTAAACCCCATCC (SEQ ID	
	•		

ı	1	NO. 660	
26	HICI (GEO ID	NO: 669)	_[
20	HIC1 (SEQ ID NO: 26)	TIGGGTTGGAGAAGAAGTTTA (SEQ ID NO: 670)	1
	·	TCATATTTCCAAAAACACACC (SEQ ID NO: 671)	
27	STMN1 (SEQ ID	GAGTTTGTATTTAAGTTGAGTGGTT	224
	NO: 27)	(SEQ ID NO: 672)	334
20		AACAAAACAATACCCCTTCTAA (SEQ ID NO: 673)	
28	STK11 (SEQ ID NO: 28)	TAAAAGAAGGATTTTTGATTGG (SEQ ID NO: 675)	528
	10.20)	CATCTTATTTACCTCCCTCCC (SEO ID	
	·	INO: 6/4)	
29 ⁻ .	ING4 (SEQ ID NO: 29)	ATTAGGGATGAGAGGATTTGTA (SEQ ID NO: 676)	212
		TCTTCCTAACCATACACACTAACC	•
20-	100 500 500	(SEQ ID NO: 677)	
30	MGMT (SEQ ID NO: 30)		636
<u> </u>	140.30)	ID NO: 678) ACCTTTTCCTATCACAAAAATAA (SEQ	;
<u> </u>		ID NO: 679)	·
31	MLH1 (SEQ ID	TAAGGGGAGAGGAGGAGTTT (SEQ ID	545
	NO: 31)	μνΟ: 080)	
		ACCAATTCTCAATCATCTCTTT (SEQ ID NO: 681)	
32	MYC (SEQ ID	AGAGGGAGTAAAAGAAAATGGT (SEO	712
i	NO: 33)	ID NO: 682)	,
	,	CCAAATAAACAAAATAACCTCC (SEQ ID NO: 683)	
33	N33 (SEO ID NO	TTTTA CATTEGA CO	
	35)	TTTTAGATTGAGGTTTTAGGGT (SEQ ID NO: 684)	497
		ATCCATTCTACCTCCTTTTTCT (SEQ ID	: <i>'</i>
		140: 083)	
34	PAX6 (SEQ ID NO: 36)	GGAGGGGAGAGGGTTATG (SEQ ID	374
	110.30)	NO: 686) TACTATACACACCCCAAAACAA (SEQ	
		ID NO: 687)	
35	X51730 PGR	TTTTGGGAATGGGTTGTAT (SEC. ID.	369
	(SEQ ID NO: 67)	INO: 746) CTACCCTTAACCTCCATCCTA	
36	PTEN (SEQ ID	(SEQ 1D NO: 747)	
50	NO: 38)	TTTTAGGTAGTTATATTGGGTATGTT (SEQ ID NO: 690)	346
		TCAACTCTCAAACTTCCATCA (SEQ ID	
		INO: 691)	,
37	RARB (SEQ ID	TTGTTGGGAGTTTTTAAGTTTT (SEQ	353
	NO: 39)	μD NO: 692)	4.
		CAAATTCTCCTTCCAAATAAAT (SEQ ID NO: 693)	
38	SFN (SEQ ID	GAAGAGACCACACCACCACCACCACCACCACCACCACCAC	180
	h =	ן או איט איז און	489
		CTATCCAÁCAAACCCAACA (SEQ ID	

<u> </u>		NO: 694)	1
39	S100A2 (SEQ ID	GTTTTTAAGTTGGAGAAGAGGA (SEQ	460
	NO: 41)	ID NO: 696)	100
		ACCTATAAATCACAACCCACTC (SEQ	'
<u> </u>		ID NO: 697)	
40	TGFBR2 (SEQ ID	GTAATTTGAAGAAAGTTGAGGG (SEQ	296
	NO: 43)	ID NO: 698)	
		CCAACAACTAAACAAAACCTCT (SEQ	
		ID NO: 699)	
41	TIMP3 (SEQ ID	TGAGAAAATTGTTGTTTGAAGT (SEQ	306
	NO: 44)	ID NO: 700)	
		CAAAATACCCTAAAAACCACTC (SEQ	
	<u>'. </u>	ID NO: 701)	
42	VHL (SEQ ID	TGTAAAATGAATAAAGTTAATGAGTG	362
	NO: 45)	(SEQ ID NO: 702)	
		TCCTAAATTCAAATAATCCTCCT (SEQ	
		ID NO: 703)	
43	CDKN1C (SEQ	GGGGAGGTAGATATTTGGATAA (SEQ	300
	ID NO: 46)	ID NO: 704)	•
		AACTACACCATTTATATTCCCAC (SEQ	
		ID NO: 705)	· .
44	CAV1 (SEQ ID	GTTAGTATGTTTGGGGGTAAAT (SEQ	435
	NO: 47)	ID NO: 707)	H33 . ,
		ATAAATAACACCTTCCACCCTA (SEQ	1.
		ID NO: 706)	
45	CDH13 (SEQ ID	TTTGTATTAGGTTGGAAGTGGT (SEQ	206
. ,	NO: 48)	ID NO: 708)	286 \
'		CCCAAATAAATCAACAACAACA (SEQ	
		ID NO: 709)	
46	NDRG1 (SEO ID	GGTTTTGGGTTTAGTGGTAAAT (SEQ	41.6
·	NO: 49)	ID NO: 711)	416
		AACTTTCATAACTCACCCTTTC (SEQ	
٠.		ID NO: 710)	İ
47	PTGS2 (SEQ ID	GATTTTTGGAGAGGAAGTTAAG (SEQ	201
		ID NO: 713)	381
		AAAACTAAAAACCAAACCCATA (SEQ	
		ID NO: 712)	
48		TOCOCOTTE A COMPANIA CONTRA	
		NO: 714)	398
	, , , , ,		
		CTTAAAAACACTAAAACTTCTCAAA (SEQ ID NO: 715)	
49	TMEFF2 (SEO ID	TTGTTTGGGTTAATAATGGAGGG	
	NO: 52)	TTGTTTGGGTTAATAAATGGA (SEQ ID	295
	1 '	NO: 716) CTTCTCTCTCTCTCCCCTCTC (SEQ ID NO: 717)	• •
50	PLAU (SEQ ID	TATTATAGGAGGATTAGA	
- -		TATTATAGGAGGATTGAGGAGG (SEQ ID NO: 718)	499
•	, ,	CCCATAAATCAM	
		CCCATAAAATCATACCACTTCT (SEQ	,
51	TMEEED (SEC ID	ID NO: 719)	<u> </u>
J I	NO: 54)	TGTTGGTTGTTGTTGTT (SEQ ID	319
	10. 34)·	NO: 720) CTTTCTACCCATCCCAAAA	
		(SEQ ID NO: 721)	,

52	DNMT1 (SEO ID	TCCCCATCACACCTAAAA (SEC ID NO	bio
J.Z.	NO: 55)	TCCCCATCACACCTAAAA (SEQ ID NO:	210
	110.33)	722) GGGAGGAGGGGATGTATT (SEQ ID NO: 723)	
53	ESR1 (SEQ ID		
,,	1 1	AGGGGGAATTAAATAGAAAGAG (SEQ	662
•	140: 70)	ID NO: 752)	
		CAATAAAACCATCCCAAATACT (SEQ	
	ADARI KORO TO	ID NO: 753)	
54	APAF1 (SEQ ID	AGATATGTTTGGAGATTTTAGGA	674
	NO: 57)	(SEQ ID NO: 726)	
•		AACTCCCCACCTCTAATTCTAT (SEQ	
		ID NO: 727)	'
55	HOXAS (SEQ ID		392
•	NO: 58)	NO: 729)	
	,	GAAGGGGAAAGTTATTTAGTTA	
<u> </u>	<u> </u>	(SEQ ID NO: 728)	.,
56	RASSF1 (SEQ ID	ACCTCTCTACAAATTACAAATTCA	347
;	NO: 59)	(SEQ ID NO: 730)	· .
1	· · · · · · · · · · · · · · · · · · ·	AGTTTGGGTTAGTTTGGGTT (SEQ ID	, ,
		NO: 731)	,
57	BRCA2 (SEQ ID	ACCCACCCAAACCTAACT (SEQ ID NO:	388
	NO: 60)	733) GGTTGGTAGAGATAAAAGGGTA	· .
	<u> </u>	(SEQ ID NO: 732)	·
58	CCND1 (SEQ ID	GATTATAGGGGAGTTTTGTTGA (SEQ.	404
	NO: 61)	ID NO: 734)	
. •		CACCTCCAACATCCAAATA (SEQ ID	· .
٠		NO: 735)	
59 .	EDNRB (SEQ ID	TCAAAACATCCTCTATCTCTCC (SEQ	484
	NO: 62)	ID NO: 737)	104
		ATAATTGGGGGTTGTATGTATT (SEQ	, .
		ID NO: 736)	,
60	EGFR (SEQ ID	GGGTTTGGTTGTAATATGGATT (SEQ	732
:	NO: 63)	ID NO: 738)	132
		CCCAACACTACCCCTCTAA (SEQ ID	
	· ·	NO: 739)	,
61	ERBB2 (SEQ ID	GAGGTAGAGGTTGTGGTGAGT (SEQ	528
	NO: 64)	ID NO: 740) TCCCAACTTCACTTTCTCC	528
		(SEQ ID NO: 741)	
62	FOS (SEQ ID	ATCCTCCACTTCTACTTCCA (SEQ ID	500
!	NO: 65)	NO: 743)	500
		TTTTAGGGTTATAGGGAAAGGT (SEQ	
		ID NO: 742)	
63	NFKB1 (SEQ ID		
00	NO: 66)	TTTGTAGAATGAAAAGTAGAGTGTG (SEQ ID NO: 744)	485
•	10.00)		
	No.	ACCTTAAAAACCCCAACAAT (SEQ ID	
64	X51730 PGR	NO: 745)	
		TTTTGGGAATGGGTTGTAT (SEQ ID	369
	(SEQ ID NO: 67)	NO: 746) CTACCCTTAACCTCCATCCTA	
65	TDE2 (CDC TO	(SEQ ID NO: 747)	
65	TP53 (SEQ ID	GAGTAGGTAGTTGTTGGGTTTC (SEQ	702
•	NO: 68)	ID NO: 748)	
		ACCCCTAATTTAACACTTCTCA (SEO	

	1.	ID NO: 749)	1
66	TP73 (SEQ ID		607
00			607
	NO: 69)	(SEQ ID NO: 750)	
	<u> </u>	GAAAAACCTCTAAAAACTACTCTCC	•
		(SEQ ID NO: 751)	
67	ESR1 (SEQ ID	AGGGGGAATTAAATAGAAAGAG (SEQ	662
	NO: 70)	ID NO: 752)	002
		CAATAAAACCATCCCAAATACT (SEQ	
	·	ID NO: 753)	
68	CEDDINET (CEO		
06	SERPINEI (SEQ	GGGGTATAGAGAGAGTTTGGAT (SEQ	492
]	ID NO: 71)	ID NO: 754)	· .
		ACAATTAAACAAACCCCAATAA (SEQ	
<u> </u>		ID NO: 755)	,
69	CALM1 (SEQ ID	AAAAACTCTAACCCTTCTCAAA (SEQ	414
	NO: 72)	ID NO: 757)	114
	. ,	TATTTTTAGTTTGGGGTGTTGT (SEQ	
		ID NO: 756)	
70	CONTROD (CITO		
/U. ;	CSNK2B (SEQ	TACCCCTCACCATTACTCTAAC (SEQ	437
l. '	ID NO: 73)	ID NO: 759)	, ,
1		TAGTTTTGTGTTTATTGGGTGA (SEQ	
	1.	ID NO: 758)	
71	FGFR1 (SEQ ID	1.00	267
	NO: 74)	ID NO: 760)	367
	μιο. / -/ /		. '
· .	· ·	CCTTTACCCTTCTCAAATCTAA (SEQ	
		ID NO: 761)	'
72	MKI67 (SEQ ID	CCAATACTCTACAACCATCAAA (SEQ	499
	NO: 75)	ID NO: 763)	
		GGGAAGTTGAAGTAGGAAGAT (SEQ.	, , ,
ľ	'	ID NO: 762)	}
73	NPM1 (SEQ ID	· 	
,,,	NO: 76)	AAGGAAGGAGGAAGTAATTTGT (SEQ	454
f	INO: 70)	ID NO: 764)	<u>.</u>
, ·		TTACACCAACCCCTAAACTAAC (SEQ	
ļ		ID NO: 765)	•
74 ·	MAPK1 (SEQ ID	TTTAGATAATTTTAGGATGGGG (SEQ	743
l	NO: 77)	ID NO: 766)	. ,
		TTCTCATTCACAAAAACAAAAA (SEQ	
ł		ID NO: 767)	.,
75	SYK (SEQ ID		
1,3		GTGGGTTTTGGGTAGTTATAGA (SEQ	485
	NO: 78)	ID NO: 768)	· · ·
1.		TAACCTCCTCTCCTTACCAA (SEQ ID	
<u> </u>	* 1	NO: 769)	
76	TK2 (SEQ ID	ATACAACCTCAAATCCTATCCA (SEQ	485
·	NO: 79)	ID NO: 771)	
1.		AGGGAGAAGGAAGTTATTTGTT (SEQ	
		ID NO: 770)	
77	HSPB1 (SEQ ID		
1′′		CCTACCTCTACCACTTCTCAAT (SEQ	216
	NO: 80)	ID NO: 773)	
1		AAGAGGGTTTAGTTTTATTTGG (SEQ	
		ID NO: 772)	
78	TES (SEQ ID	AGGTTGGGGATTTTAGTTTTT (SEQ ID	110 /
1	NO: 81)	NO: 774)	1140
ــــــــــــــــــــــــــــــــــــــ	<u> </u>	<u> </u>	1 "

•		•	
		ACCTTCTTCACTTTATTTTCCA (SEQ ID NO: 775)	
79	SDC4 (SEQ ID	CCTAACTACCCTCATTCCTTT (SEQ ID	269
		NO: 777) AGTTGGGGAAATTAAGGTTTAG (SEQ	
	·	ID NO: 776)	
0	PITX2 (SEQ ID NO: 83)	TCCTCAACTCTACAAACCTAAAA (SEQ ID NO: 779)	408
•		GTAGGGGAGGGAAGTAGATGT (SEQ ID NO: 778)	
1		ACTTATTTTCTTTTCCTCTAAAAAC	489
		(SEQ ID NO: 781)	
		TATGGTTTGGTGAGGGTATATT (SEQ ID NO: 780)	·
2	FGF1 (SEQ ID	AGTTGTGTTTAATTGGGAAGAG (SEO	420
	NO: 85)	ID NO: 782)	
· ; ·	1	CTTATCCCATCCACTATACCAT (SEQ	
3	CDINOD (SEC ID	ID NO: 783)	
. د :	NO: 86)	ATAGTTTGTGGTTTGGATTTTT (SEQ ID NO: 784)	435
	110.80)	AAAACCTTTCCCTAACTTCAAT (SEQ	
		ID NO: 785)	٠,
4	CTSB (SEQ ID	AAAATTCCATCAAATAACCATAA	450
. ,	NO: 87)	(SEQ ID NO: 787)	, ,
• •		AAAAAGGAAGGTAGTAGGATTGT (SEQ ID NO: 786)	
35	CTSD (SEQ ID	ATACAACCCTCCAACCTTCTAC (SEQ	498
. :	NO: 88)	ID NO: 789)	170
		AAGGGGTTTTTAAGGAAATG (SEQ ID NO: 788)	
36 .	PLAUR (SEQ ID	TGGTTAAAATGGAGGGTTTAAT (SEQ	348
•	NO: 89)	ID NO: 790)	540
		CCCCAAATTACCTAAATACAAA (SEQ	
		ID NO: 791)	
37	PSA (SEQ ID	TAAGAGAGAGGAGTTGAGGTTT (SEQ	478
	NO: 90)	ID NO: 792) CCAAAATTAACCACCTACCTAA (SEQ	
		ID NO: 793)	
38	CGA (SEQ ID	TAGTGGTATAAGTTTGGAAATGTT	364
	NO: 91)	(SEQ ID NO: 794)	
		TCCACCTACATCTAAACCCTAA (SEQ	
	CVD2D4 (SEQ II	ID NO: 795)	
9 .	NO: 92)	TAAGGGTTTGGAGTAGGAAGTA (SEQ ID NO: 796)	403
•	110.52)	CACATACAACAAAATTACCCAA (SEQ	
	CVD2 4 4 CD C	ID NO: 797)	
90	NO: 93) ,	TATCACCACCTTCCCATATTTA (SEQ	484.
	μνο. 93) ,	ID NO: 799) GTTTGATGAATGGATTGTATGA (SEC	
	<u> </u>	GTTTGATGAATGGATTGTATGA (SEQ ID NO: 798)	
91	TK1 (SEQ ID	ACCTCTACAAACATCTTATTCCA (SEC) 487

		•	•
	NO: 94)	ID NO: 801)	1
		TTGGGGGAGTTAGGTAGTATAG (SEQ	
		ID NO: 800)	
92	RENBP (SEQ ID		
	NO: 95)	TTTGGTAGGGTTAAGGTTTTTA (SEQ ID NO: 802)	350
	10. 55)	CTTA CTCA TCC CTC	
		CTTACTCÁTCCCTCCTACTCC (SEQ ID	1
02	E10 (CDC TD 270	NO: 803)	
93	F12 (SEQ ID NO:	TAGGTTTAGGAGGGTAGTTTGA (SEQ	450
	96)	μD NO: 804)	
	· ·	CTCTCACAACCCAAAAATACA (SEQ	
		ID NO: 805)	
94	REN (SEQ ID	ACCTACTCCAAAAATCACAAAA (SEQ	480
	NO: 97)	ID NO: 807)	107
٠.		TATGTGGAAAAGTTAGGGTGTT (SEQ	
		ID NO: 806)	'
95	EBAG9 (SEQ ID		460
	NO: 98)	NO: 809)	463
		AATGTTTTAGAGGTTAGGGTTG (SEQ ID NO: 808)	,
96	MCMD (CEO ID		•
•	MSMB (SEQ ID	GTTTTGTAGGATGGTTTGATTT (SEQ	324
	NO: 99)	ID NO: 810)	
		TATATTTACCTTATCCCCACCC (SEQ	,
^		ID NO: 811)	1
97	X15323	AAACTCTCCCCTACCCTCTAC (SEQ ID	374
	angiotensinogen	INO: 813)	
	gene 5'region and	GATGGAGTTGTTTTTAGGTTGT (SEQ	∤
	exon 1 (SEQ ID.	ID NO: 812)	•
	NO: 100)		,
98	ZNF147 (SEO ID	TTTGTGTAAATAAGATGTGGGA (SEQ	40.4
٠.	NO: 101)	ID NO: 814)	484
	· · · · · · · · · · · · · · · · · · ·	TAAACCCCTACAAAACTACCAA (SEQ	
•	• .	ID NO: 815)	
99.	EBBP (SEQ ID	GTATTTCTTTTTCGTC	
	NO: 102)	GTATTTGTTTTTGGTGAGGGT (SEQ ID	482
•	140. 102)	μνο. 616)	
		ATCATCTTCCTAAACATTCCAA (SEQ	
100	CAT D (CDC TD	ID NO: 817)	
100	CALR (SEQ ID	TAAATCACAACCATTAACCAAA (SEQ	490
	NO: 103)	ID NO: 819)	
		ATAAGAGGGGAGGAAGGTTTA (SEQ	1,
	,	ID NO: 818)	
101	BCAR1 (SEQ ID	AATTCTTCCTTCTATCTCCCTC (SEQ ID	400
	NO: 104)	NO: 821) TTTATTTTTGGGAAGGTTGTT	
		(SEQ ID NO: 820)	
102	COX7A2L (SEQ	A A TOOTA A A A A A CONTRACTOR	, , , , , , , , , , , , , , , , , , ,
	ID NO: 105)	(SEQ ID NO: 823)	398
		GGAGGTGTA AGGAGA ATLACA CA	.
	,	GGAGGTGTAAGGAGAATAGAGA (SEQ ID NO: 822)	
103	AF174646	CCA A TTCA TCA TCA	
. 0.5		CCAATTCATCATTCAACATCTA (SEQ	325
		ID NO: 825)	
	kallikrein gene,	ATTTATTTGGGAGGATAGTGG (SEQ ID	
	promoter region	NO: 824)	

	•	- 34 -	•
i	h. d		,
	and partial		1.
	sequence (SEQ I NO: 106)	D	
104	KLK3 (SEQ ID	TTCC + CMCM	ŀ
104	NO: 107)	TTGGAGTGTAAAGGATTTAGGT (SEQ	387
1	110. 107)	μυ ΝΟ: 826)	
		AACCCACATAATAACACAACTCT	F
105	AKR1B1 (SEQ	(SEQ ID NO: 827)	
	ID NO: 108)	CAACAAAACATTCTTCTAAACTC (SEQ ID NO: 829)	446
		AGGTATTTAATTTTAGGATGGGT (SEC	
		ID NO: 828)	2
106	TGM4 (SEQ ID	AATCCTAACTTTTAATCACCCA (SEQ	105
	NO: 109)	μυ NO; 831) ;	435
		GAGAGGGTAATGGTTTTAGGTA (SEQ	ĺ.
105	<u> </u>	W NO: 8301	
107	AR (SEQ ID NO	: AATATAGGGAGGTTTAGGGTTT (SEQ	424
	[110]	μυ ΝΟ: 832)	724
		TAACCATACATTTCTCATCCAA (SEQ	
108	HCDA1A CORC	_ INU: 833)	ļ
100	HSPA1A (SEQ	AACCTTTCAAATTCACAATCA (SEQ ID	495
	ID NO: 111)	PIO. 022) COATTTATTGGAGGGGATAG	
109	FKBD4 (SEC.TD	<u>(SEQ ID NO: 834)</u>	ı
109	FKBP4 (SEQ ID NO: 112)	TTTTTAAGTAGGGAAGGGTTT (SEQ ID	308
	112)	Property Control AACTACCTACCCC	1
110	ESR2 (SEQ ID	(SEQ ID NO: 837)	
	NO: 113)	AAACCTTCCCAATAACCTCTTA (SEQ ID NO: 839)	471
	1	ш NO: 839)	
<u>.</u>		TAGAGGGGAGTAGTGTTTGAGT (SEQ ID NO: 838)	
111.	IGF1 (SEQ ID	TACCCTTCTCCCAAAATTA	
	NO: 114)	ID NO: 841)	402
		GTATTAAAGGAATATGGGGGAT (SEQ	
		ID NO: 840)	-
112	VTN (SEQ ID	GTTATTTGGGTTAATGTAGGGA (SEQ	492
	NO: 115)	INO: 842)	T74
•	'	TCTATCCCCTCAAACTTAAAAA (SEQ	,
113	CTGT: (GDC: TD	<u>μυ NO: 843)</u>	
Ϋ́	CTSL (SEQ ID NO: 116)	CTACACCCACCCTTAAATAAAA (SEQ	328
	110)	μD NO: 845)	
	1	TTAGTGGATTTGGAGGAAGTAG (SEQ ID NO: 844)	
14	TGFB3 (SEQ ID		
•	NO: 117)	CCTACTAAAAATCAAAACCCAA (SEQ : ID NO: 847)	369
		AAGGTGGTGTAAGTGGATAGAG (SEQ	, ,
		ID NO: 846)	
15	MAPKAPK5	AAACCTACCTCCCCAACCT	10.5
	(SEQ ID NO:	NO: 849)	195
		ATTTTTGGTTTTAGGGTTGTAA (SEQ	•
1.6		ID NO: 848)	
16	PCAF (SEQ ID	GGATAAATGATTGAGAGGTTGT (SEO	60
<u>. </u>	NO: 119)	ID NO: 850)	. · ·
٠.			_, <u> </u>

		CCTCCCTTAATTCTCCTACC (SEQ ID NO: 851)	
11.7	μιο. 120)	NO: 852)	330
110	<u></u>	CCTAACCCTACCCTTAATTTTT (SEQ ID NO: 853)	
118	F. (0. 121)	855)	i i
	·	GATAGAAGGATTTTAGTTTTATTGTT (SEQ ID NO: 854)	

Table 2: Hybridisation oligonucleotides according to Example 2.

No:	Gene	Oligo:
1	ELK1 (SEQ ID NO: 10)	GTTTACGCGGAGTTTAGT (SEQ ID NO: 856)
2	ELK1 (SEQ ID NO: 10)	GTTTATGTGGAGTTTAGT (SEQ ID NO: 857)
3	ELK1 (SEQ ID NO: 10)	GTAGTATGGCGTGCGATA (SEQ ID NO: 858)
4	ELK1 (SEQ ID NO: 10)	GTAGTATGGTGTGATA (SEQ ID NO: 859)
5	ELK1 (SEQ ID NO: 10)	TTAATCGGCGTGGAGTAT (SEQ ID NO: 860)
5 ,	ELK1 (SEQ ID NO: 10)	TTAATTGGTGTGGAGTAT (SEQ ID NO: 861)
7	GP1BB (SEQ ID NO: 7)	TTTGAGAGCGGGTGGGAG (SEQ ID NO: 862)
3	GP1BB (SEQ ID NO: 7)	TTTGAGAGTGGGTGGGAG (SEQ ID NO: 863)
)	GP1BB (SEQ ID NO: 7)	TTGGTTAGGTCGTAGTAT (SEQ ID NO: 864)
10	GP1BB (SEQ ID NO: 7)	TTGGTTAGGTTGTAGTAT (SEQ ID NO: 865)
1	GP1BB (SEQ ID NO: 7)	GTGGGAGCGGAAGTTTGA (SEQ ID NO: 866)
.2 .	GP1BB (SEQ ID NO: 7)	GTGGGAGTGGAAGTTTGA (SEQ ID NO: 867)
3	GP1BB (SEQ ID NO: 7)	TGTTGGTGAACGTCGTAG (SEQ ID NO: 868)
4	GP1BB (SEQ ID NO: 7)	TGTTGGTGAATGTTGTAG (SEQ ID NO: 869)
5		GGAGTTCGGTCGGGTTTT (SEQ ID NO: 870)
6	GP1BB (SEQ ID NO: 7)	GGAGTTTGGTTGGGTTTT (SEQ ID NO: 871)
7	··	TAGGTCGATTCGGGTTGA (SEQ ID NO: 872)
8	GP1BB (SEQ ID NO: 7)	TAGGTTGATTTGGGTTGA (SEQ ID NO: 873)

	•	- 36 -
I	1.	
19	WT1 (SEQ ID	TAGTGAGACGAGGTTTTT (SEQ ID NO: 874)
20 .	NO: 8)	
20 .	WT1 (SEQ ID NO: 8)	TAGTGAGATGAGGTTTTT (SEQ ID NO: 875)
21	WT1 (SEQ ID	ATTCAGGGAGG
	NO: 8)	ATTGAGGGACGTTCGTTT (SEQ ID NO: 876)
22	WT1 (SEQ ID	ATTGAGGGATGTTTGTTT (SEQ ID NO: 877)
	NO: 8)	(SEQ ID NO: 877)
23	WT1 (SEQ ID	GTATTCGATTTTGTTCGGA (SEQ ID NO: 878)
	NO: 8)	
24	WT1 (SEQ ID	GTATTTGATTTTGGA (SEQ ID NO: 879)
25	NO: 8)	<u> </u>
دے	WT1 (SEQ ID NO: 8)	GTAGGCGGTAATCGTTTT (SEQ ID NO: 880)
26	WT1 (SEQ ID	
	NO: 8)	GTAGGTGGTAATTGTTTT (SEQ ID NO: 881)
27	APC (SEQ ID	
	NO: 11):	GGGTTTCGTTTAATCGTAT (SEQ ID NO: 882)
28 -	APC (SEQ ID	<u> </u>
	NO: 11)	GGGTTTTGTTTAATTGTAT (SEQ ID NO: 883)
29	APC (SEQ ID	GGTTCGTATTTAGCGGATT (SEQ ID NO: 884)
	NO: 11)	<u> </u>
0	APC (SEQ ID	GGTTTGTATTTAGTGGATT (SEQ ID NO: 885)
11	NO: 11)	<u></u>
, 1	APC (SEQ ID. NO: 11)	TAGTTAATCGGCGGGTTT (SEQ ID NO: 886)
2	APC (SEQ ID	
	NO: 11)	TAGTTAATTGGTGGGTTT (SEQ ID NO: 887)
3	APC (SEQ ID	TTTTCGAGTTCGGTAGTAT (CDC TO TO TO TO TO TO TO TO TO TO TO TO TO
• .	NO: 11)	TTTTCGAGTTCGGTAGTAT (SEQ ID NO: 888)
4	APC (SEQ ID	TTTTTGAGTTTGGTAGTAT (SEQ ID NO: 889)
	NO: 11)	
5	ARHI (SEQ ID	TTTTCGAGTAGCGTATTTG (SEQ ID NO: 890)
6	NO: 12)	<u> </u>
	ARHI (SEQ ID NO: 12)	TTTTTGAGTAGTGTATTTG (SEQ ID NO: 891)
7 .	ARHI (SEQ ID	
	NO: 12)	ATAAGTGTGCGAGTTTAA (SEQ ID NO: 892)
3	ARHI (SEQ ID	
	NO: 12)	ATAAGTGTGTGAGTTTAA (SEQ ID NO: 893)
θ,	ARHI (SEQ ID	TATAGTTGCGTAGGTAGT (SEQ ID NO: 894)
	_NO: 12)	[
)	ARHI (SEQ ID	TATAGTTGTGTAGGTAGT (SEQ ID NO: 895)
·	NO: 12)	<u>1 </u>
٠.	BCL2 (SEQ ID	TGTTTCGCGTGATTGAAG (SEQ ID NO: 896)
` ;	NO: 13)	<u> </u>
	BCL2 (SEQ ID NO: 13)	TGTTTTGTGTGATTGAAG (SEQ ID NO: 897)
		<u></u>
	NO: 13)	AGGGTACGATAATCGGGA (SEQ ID NO: 898)

44	BCL2 (SEQ ID NO: 13)	AGGGTATGATAATTGGGA (SEQ ID NO: 899)
45		GGATTCGGTCGTTAGGAT (SEQ ID NO: 900)
46	BCL2 (SEQ ID NO: 13)	GGATTTGGTTAGGAT (SEQ ID NO: 901)
47.	NO: 13)	GATTTCGTCGAGATGTTTA (SEQ ID NO: 902).
48	NO: 13)	GATTTTGTTGAGATGTTTA (SEQ ID NO: 903)
49 .	NO: 14)	ATAAGCGCGTATAGGTTTT (SEQ ID NO: 904)
50	NO: 14)	ATAAGTGTGTATAGGTTTT (SEQ ID NO: 905)
51	NO: 14)	TTTCGTAACGTATGTTGGA (SEQ ID NO: 906)
52	NO: 14)	TTTTGTAATGTATGTTGGA (SEQ ID NO: 907)
53	BRCA1 (SEQ ID NO: 14)	AATAAGTCGTAATTGGAAG (SEQ ID NO: 908)
54	NO: 14)	AATAAGTTGTAATTGGAAG (SEQ ID NO: 909)
55	NO: 14)	TTTACGTTATTCGGGGGTA (SEQ ID NO: 910)
56	BRCA1 (SEQ ID NO: 14)	TTTATGTTATTTGGGGGTA (SEQ ID NO: 911)
57	CALCA (SEQ ID NO: 15)	TATAGCGGCGGAATAAG (SEQ ID NO: 912)
58	CALCA (SEQ ID NO: 15)	TATAGTGGTGGGAATAAG (SEQ ID NO: 913)
59	NÓ: 15)	TTGTTAGTTCGCGATTTATA (SEQ ID NO: 914)
60 :	CALCA (SEQ ID NO: 15)	TTGTTAGTTTGTGATTTATA (SEQ ID NO: 915)
61	CALCA (SEQ III NO: 15)	TTTAGGGATCGCGTATAGA (SEQ ID NO: 916)
62	NO: 15)	TTTAGGGATTGTGTATAGA (SEQ ID NO: 917)
63	NO: 15)	AAATTTTTCGTAGACGGTG (SEQ ID NO: 918)
64	NO: 15)	AAATTTTTGTAGATGGTG (SEQ ID NO: 919)
65	NO: 16)	GGATCGCGTTTGAAGTTG (SEQ ID NO: 920)
66	NO: 16)	GGATTGTGTTTGAAGTTG (SEQ ID NO: 921)
67	NO: 16)	TTTTAATAACGAGAGGGG (SEQ ID NO: 922)
68	CCND2 (SEQ II NO: 16)	TTTTAATAATGAGAGGGG (SEQ ID NO: 923)

69	CCND2 (SEQ ID NO: 16)	TATCGTTTTAGAGCGGAGA (SEQ ID NO: 924)
70		TATTGTTTTAGAGTGGAGA (SEQ ID NO: 925)
71	CDH1 (SEQ ID NO: 17)	TTGGGATTCGAATTTAGT (SEQ ID NO: 926)
72	CDH1 (SEQ ID NO: 17)	TTGGGATTTGAATTTAGT (SEQ ID NO: 927)
73	CDH1 (SEQ ID NO: 17)	GAGGGTTATCGCGTTTAT (SEQ ID NO: 928)
74	CDH1 (SEQ ID NO: 17)	GAGGGTTATTGTGTTTAT (SEQ ID NO: 929)
75	CDH1 (SEQ ID NO: 17)	TTAATTAGCGGTACGGGG (SEQ ID NO: 930)
76	CDH1 (SEQ ID NO: 17)	TTAATTAGTGGTATGGGG (SEQ ID NO: 931)
77	CDH1 (SEQ ID NO: 17)	TTTAGTGGCGTCGGAATT (SEQ ID NO: 932)
78	CDH1 (SEQ ID NO: 17)	TTTAGTGGTGTTGGAATT (SEQ ID NO: 933)
79	CDKN1B (SEQ ID NO: 18)	GTTATAATTTCGGGAAAGA (SEQ ID NO: 934)
80	CDKN1B (SEQ ID NO: 18)	GTTATAATTTTGGGAAAGA (SEQ ID NO: 935)
81	CDKN1B (SEQ ID NO: 18)	GGACGAGTTTTTATACGTAG (SEQ ID NO: 936)
82	CDKN1B (SEQ ID NO: 18)	GGATGAGTTTTTATATGTAG (SEQ ID NO: 937)
83	CDKN1B (SEQ ID NO: 18)	TTTGATTTCGAGGGGAGT (SEQ ID NO: 938)
84	CDKN1B (SEQ ID NO: 18)	TTTGATTTTGAGGGGAGT (SEQ ID NO: 939)
85	CDKN1B (SEQ ID NO: 18)	AAGAGAAACGTTGGAATA (SEQ ID NO: 940)
86	CDKN1B (SEQ ID NO: 18)	AAGAGAAATGTTGGAATA (SEQ ID NO: 941)
87.	CDKN1B (SEQ ID NO: 18)	TAGTATCGGACGTTAGGAT (SEQ ID NO: 942)
88	CDKN1B (SEQ ID NO: 18)	TAGTATTGGATGTTAGGAT (SEQ ID NO: 943)
89	CDKN2A (SEQ ID NO: 19)	TTTTTAGTCGTATAGGTGA (SEQ ID NO: 944)
90	CDKN2A (SEQ ID NO: 19)	TTTTTAGTTGTATAGGTGA (SEQ ID NO: 945)
91	CDKN2A (SEQ ID NO: 19)	GTTGTATCGCGGAGGAAG (SEQ ID NO: 946)
92	CDKN2A (SEQ ID NO: 19)	GTTGTATTGTGGAGGAAG (SEQ ID NO: 947)
93 ,	CDKN2A (SEQ ID NO: 19)	ATTCGTTAAGTGTTCGGAG (SEQ ID NO: 948)

94	CDKN2A (SEQ ID NO: 19)	ATTTGTTAAGTGTTTGGAG (SEQ ID NO: 949)
95	CDKN2A (SEQ ID NO: 19)	GAAAGATATCGCGGTTTTT (SEQ ID NO: 950)
96	CDKN2A (SEQ ID NO: 19)	GAAAGATATTGTGGTTTTT (SEQ ID NO: 951)
97	CDKN2A (SEQ ID NO: 19)	TTTCGTTAGTATCGGAGG (SEQ ID NO: 952)
98	CDKN2A (SEQ ID NO: 19)	TTTTGTTAGTATTGGAGG (SEQ ID NO: 953)
99.	CDKN2A (SEQ ID NO: 19)	GGAGTTTTCGGTTGATTG (SEQ ID NO: 954)
100	CDKN2A (SEQ ID NO: 19)	GGAGTTTTTGGTTGATTG (SEQ ID NO: 955)
101	CDKN2A (SEQ ID NO: 19)	GGGCGTTGTTTAACGTAT (SEQ ID NO: 956)
102	CDKN2A (SEQ ID NO: 19)	GGGTGTTGTTTAATGTAT (SEQ ID NO: 957)
103	CDKN2A (SEQ ID NO: 19)	AATAGTTACGGTCGGAGG (SEQ ID NO: 958)
104	CDKN2A (SEQ ID NO: 19)	AATAGTTATGGTTGGAGG (SEQ ID NO: 959)
105	CDKN2A (SEQ ID NO: 19)	GGTCGGAGGTCGATTTAG (SEQ ID NO: 960)
106	CDKN2A (SEQ ID NO: 19)	GGTTGGAGGTTGATTTAG (SEQ ID NO: 961)
107	CDKN2B (SEQ ID NO: 20)	GGTTTTTCGGCGATTATAG (SEQ ID NO: 962)
108	CDKN2B (SEQ ID NO: 20)	GGTTTTTTGGTGATTATAG (SEQ ID NO: 963)
109	CDKN2B (SEQ ID NO: 20)	AAAGTTCGGAGTTAACGAT (SEQ ID NO: 964)
110	CDKN2B (SEQ ID NO: 20)	AAAGTTTGGAGTTAATGAT (SEQ ID NO: 965)
111	CDKN2B (SEQ ID NO: 20)	AGTTTACGGTTAACGGTG (SEQ ID NO: 966)
112	CDKN2B (SEQ ID NO: 20)	AGTTTATGGTTAATGGTG (SEQ ID NO: 967)
113	CDKN2B (SEQ ID NO: 20)	AATGCGCGAGGAGAATAA (SEQ ID NO: 968)
114	CDKN2B (SEQ ID NO: 20)	AATGTGTGAGGAGAATAA (SEQ ID NO: 969)
115	CD44 (SEQ ID NO: 21)	AAGGTTTTACGGTTCGGT (SEQ ID NO: 970)
116	CD44 (SEQ ID NO: 21)	AAGGTTTTATGGTTTGGT (SEQ ID NO: 971)
117	CD44 (SEQ ID NO: 21)	GTGGGGTTCGGAGGTATA (SEQ ID NO: 972)
118	CD44 (SEQ ID NO: 21)	GTGGGGTTTGGAGGTATA (SEQ ID NO: 973)

119	CD44 (SEQ ID NO: 21)	GGTATTTCGCGATATTTTAG (SEQ ID NO: 974)	ļ
120	CD44 (SEQ ID NO: 21)	GGTATTTTGTGATATTTTAG (SEQ ID NO: 975)	
121	CD44 (SEQ ID NO: 21)	GTTCGTTTCGGATATTATGG (SEQ ID NO: 976)	. ,
122	CD44 (SEQ ID NO: 21)	GTTTGTTTTGGATATTATGG (SEQ ID NO: 977)	
123,	CD44 (SEQ ID NO: 21)	TTTGGCGTAGATCGGTGA (SEQ ID NO: 978)	
124	CD44 (SEQ ID NO: 21)	TTTGGTGTAGATTGGTGA (SEQ ID NO: 979)	. ,
125	CSPG2 (SEQ ID NO: 22)	TTGGGTAACGTCGAATTT (SEQ ID NO: 980)	•
126	CSPG2 (SEQ ID NO: 22)	TTGGGTAATGTTGAATTT (SEQ ID NO: 981)	
127	CSPG2 (SEQ ID NO: 22)	TAATAAGTCGTTTTTTAAGG (SEQ ID NO: 982)	
128	CSPG2 (SEQ ID NO: 22)	TAATAAGTTGTTTTTTAAGG (SEQ ID NO: 983)	
129	CSPG2 (SEQ ID NO: 22)	AAAATTCGCGAGTTTAGAAA (SEQ ID NO: 984)	
130	CSPG2 (SEQ ID NO: 22)	AAAATTTGTGAGTTTAGAAA (SEQ ID NO: 985)	
131	DAPK1 (SEQ ID NO: 23)	GAAGGGAGCGTATTTTAT (SEQ ID NO: 986)	
132	DAPK1 (SEQ ID NO: 23)	GAAGGGAGTGTATTTTAT (SEQ ID NO: 987)	: _
133	DAPK1 (SEQ ID NO: 23)	TGTTTTTCGGAAATTTGT (SEQ ID NO: 988)	
134	DAPK1 (SEQ ID NO: 23)	TGTTTTTTGGAAATTTGT (SEQ ID NO: 989)	
135		TTTCGTTTCGAGATGTGTA (SEQ ID NO: 990)	•
136	DAPK1 (SEQ ID NO: 23)	TTTTGTTTTGAGATGTGTA (SEQ ID NO: 991)	· ·
137	DAPK1 (SEQ ID NO: 23)	GGAAATACGGTTTTTTCGTT (SEQ ID NO: 992)	
138	DAPK1 (SEQ ID NO: 23)	GGAAATATGGTTTTTTTGTT (SEQ ID NO: 993)	
139	GGT1 (SEQ ID NO: 24)	TATATTATCGGTTTTAGGTT (SEQ ID NO: 994)	
140	GGT1 (SEQ ID NO: 24)	TATATTATTGGTTTTAGGTT (SEQ ID NO: 995)	•
141	GGT1 (SEQ ID NO: 24)	GGGATTTTATTCGTAGATTA (SEQ ID NO: 996)	
142	GGT1 (SEQ ID NO: 24)	GGGATTTTATTTGTAGATTA (SEQ ID NO: 997)	 ,
143	GGT1 (SEQ ID NO: 24)	GAGGTTAGACGTTTTGTA (SEQ ID NO: 998)	

144	GGT1 (SEQ ID NO: 24)	GAGGTTAGATGTTTTGTA (SEQ ID NO: 999)
145		FAGATATCGTTTTTTGTGG (SEQ ID NO: 1000)
146		FAGATATTGTTTTTTGTGG (SEQ ID NO: 1001)
147		GGTTTTTTCGGTTAGTTG (SEQ ID NO: 1002)
148	GSTP1 (SEQ ID NO: 25)	GGTTTTTTTGGTTAGTTG (SEQ ID NO: 1003)
149	NO: 25)	ITTTAGGGCGTTTTTTTG (SEQ ID NO: 1004)
150	GSTP1 (SEQ ID NO: 25)	TTTTAGGGTGTTTTTTTG (SEQ ID NO: 1005)
151	NO: 25)	AGTTCGCGGGATTTTTTA (SEQ ID NO: 1006)
152	GSTP1 (SEQ ID NO: 25)	AGTTTGTGGGATTTTTTA (SEQ ID NO: 1007)
153	NO: 25)	TAGTTTTCGTTATTAGTGAG (SEQ ID NO: 1008)
154	GSTP1 (SEQ ID NO: 25)	TAGTTTTTGTTATTAGTGAG (SEQ ID NO: 1009)
155 .	HIC1 (SEQ ID NO: 26)	GAAGTTTACGCGGGATTT (SEQ ID NO: 1010)
156	HIC1 (SEQ ID NO: 26)	GAAGTTTATGTGGGATTT (SEQ ID NO: 1011)
157	NO: 26) ₁	TAAAACGGCGTATAGGGG (SEQ ID NO: 1012)
158	HIC1 (SEQ ID NO: 26)	TAAAATGGTGTATAGGGG (SEQ ID NO: 1013)
159	HIC1 (SEQ ID NO: 26)	TTTTAGTCGTTTTGATGAT (SEQ ID NO: 1014)
160	NO: 26)	TTTTAGTTGTTTTGATGAT (SEQ ID NO: 1015)
161	HIC1 (SEQ ID NO: 26)	TAGGAGATTCGAAAGTTTA (SEQ ID NO: 1016)
162	HIC1 (SEQ ID NO: 26)	TAGGAGATTTGAAAGTTTA (SEQ ID NO: 1017)
163	STMN1 (SEQ ID NO: 27)	GTTATCGGTTCGGGAATT (SEQ ID NO: 1816)
164	STMN1 (SEQ ID NO: 27)	GTTATTGGTTTGGGAATT (SEQ ID NO: 1817)
165	STMN1 (SEQ ID NO: 27)	
166	STMN1 (SEQ ID NO: 27)	
167	NO: 27)	AGAAATTACGATGATGTTAT (SEQ ID NO: 1820)
168	STMN1 (SEQ ID NO: 27)	AGAAATTATGATGATGTTAT (SEQ ID NO: 1821)

169	STMN1 (SEQ ID NO: 27)	ATGGGTGATACGTCGGTG (SEQ ID NO: 1822)
170.	STMN1 (SEQ ID	ATGGGTGATATGTTGGTG (SEQ ID NO: 1823)
171	NO: 27) STK11 (SEQ ID NO: 28)	GGGTTAAGCGTCGATTAAT (SEQ ID NO: 1018)
172	STK11 (SEQ ID NO: 28)	GGGTTAAGTGTTGATTAAT (SEQ ID NO: 1019)
173	STK11 (SEQ ID NO: 28)	AGGGAGGTCGTTGGTATT (SEQ ID NO: 1020)
174	STK11 (SEQ ID NO: 28)	AGGGAGGTTGTTGGTATT (SEQ ID NO: 1021)
175	STK11 (SEQ ID NO: 28)	GGTATTCGTGATTTACGATT (SEQ ID NO: 1022)
176	STK11 (SEQ ID NO: 28)	GGTATTTGTGATTTATGATT (SEQ ID NO: 1023)
177	STK11 (SEQ ID NO: 28)	TTTCGAGTTTTATCGAGGT (SEQ ID NO: 1024)
178	STK11 (SEQ ID NO: 28)	TTTTGAGTTTTATTGAGGT (SEQ ID NO: 1025)
179	STK11 (SEQ ID NO: 28)	ATTAATGAGCGCGTTGTAT (SEQ ID NO: 1026)
180	STK11 (SEQ ID NO: 28)	ATTAATGAGTGTGTTGTAT (SEQ ID NO: 1027)
181	ING4 (SEQ ID NO: 29)	TAGTGACGAGAAGGTTAT (SEQ ID NO: 1028)
182	ING4 (SEQ ID NO: 29)	TAGTGATGAGAAGGTTAT (SEQ ID NO: 1029)
183	ING4 (SEQ ID NO: 29)	AATTATGAAGCGGTTTTG (SEQ ID NO: 1030)
184	ING4 (SEQ ID NO: 29)	AATTATGAAGTGGTTTTG (SEQ ID NO: 1031)
185	ING4 (SEQ ID NO: 29)	TTAGAGACGTGTTTTGAA (SEQ ID NO: 1032)
186	ING4 (SEQ ID NO: 29)	TTAGAGATGTGTTTTGAA (SEQ ID NO: 1033)
187	MGMT (SEQ ID NO: 30)	TTAGGTTATCGGTGATTG (SEQ ID NO: 1034)
188	MGMT (SEQ ID NO: 30)	TTAGGTTATTGGTGATTG (SEQ ID NO: 1035)
189	MGMT (SEQ ID NO: 30)	TTTGGACGGTATCGTTTAT (SEQ ID NO: 1036)
190	MGMT (SEQ ID NO: 30)	TTTGGATGGTATTGTTTAT (SEQ ID NO: 1037)
191	MGMT (SEQ ID NO: 30)	TAGTCGTTTCGAGTAGGAT (SEQ ID NO: 1038)
192	MGMT (SEQ ID NO: 30)	TAGTTGTTTTGAGTAGGAT (SEQ ID NO: 1039)
193	MGMT (SEQ ID NO: 30)	AGTAGGATCGGGATTTTT (SEQ ID NO: 1040)

		- 43 -
194	MGMT (SEQ ID NO: 30)	(SEQ ID NO: 1041)
195	MGMT (SEQ ID NO: 30)	TTATTCGGGTACGTGGTA (SEQ ID NO: 1042)
196 197	MGMT (SEQ ID NO: 30)	TTATTTGGGTATGTGGTA (SEQ ID NO: 1043)
197	MLH1 (SEQ ID NO: 31) MLH1 (SEQ ID	ATAACTTCGGTTTCGGTAT (SEQ ID NO: 1044)
199	NO: 31) MLH1 (SEQ ID	ATAAGTTTGGTTTTGGTAT (SEQ ID NO: 1045)
200	NO: 31) MLH1 (SEQ ID	AAGAGTGGATAGTGATTT (SEQ ID NO: 1046)
201	NO: 31) MLH1 (SEQ ID	AAGAGTGGATAGTGATTT (SEQ ID NO: 1047) GAACGTGAGTACGAGGTA (SEQ ID NO: 1048)
202	NO: 31) MLH1 (SEQ ID	GAATGTGAGTATGAGGTA (SEQ ID NO: 1048)
203	NO: 31) MLH1 (SEQ ID	TAAAATGTCGTTCGTGGT (SEQ ID NO: 1050)
204	NO: 31) MLH1 (SEQ ID NO: 31)	TAAAATGTTGTTGTGGT (SEQ ID NO: 1051)
205	CA9 (SEQ ID NO: 32)	TATGGTTTCGATAATTTTTT (SEQ ID NO: 1052)
206	CA9 (SEQ ID NO: 32)	TATGGTTTTGATAATTTTTT (SEQ ID NO: 1053)
207	CA9 (SEQ ID NO: 32)	ATATATCGTGTGTTGGGA (SEQ ID NO: 1054)
208	CA9 (SEQ ID NO: 32)	ATATATTGTGTGTTGGGA (SEQ ID NO: 1055)
209	CA9 (SEQ ID NO: 32)	ATAGTTAGTCGTATGGTTT (SEQ ID NO: 1056)
210	CA9 (SEQ ID NO: 32)	ATAGTTAGTTGTATGGTTT (SEQ ID NO: 1057)
112	MYC (SEQ ID NO: 33) MYC (SEQ ID	GGGATCGCGTTGAGTATA (SEQ ID NO: 1058)
13	NO: 33) MYC (SEQ ID	GGGATTGTGTTGAGTATA (SEQ ID NO: 1059)
14	NO: 33) MYC (SEQ ID	GAGATTTGGAGTGAATAG (SEQ ID NO: 1060)
.15	NO: 33) MYC (SEQ ID	GAGATTTGGAGTGAATAG (SEQ ID NO: 1061) AGTTAGCGGTTCGTAATTT (SEQ ID NO: 1062)
16	NO: 33) MYC (SEQ ID	AGTTAGTGGTTTGTAATTT (SEQ ID NO: 1062)
17	MYC (SEQ ID	GAGTAAGGACGCGATTTT (SEQ ID NO: 1063)
18	10.33)	GAGTAAGGATGTGATTTT (SEQ ID NO: 1065)

la	Lasta III	
219	[]	:TTGGTTCGGGAAAGGTAA (SEQ ID NO: 1066)
220	100 /	:TTGGTTTGGGAAAGGTAA (SEQ ID NO: 1067)
221	N33 (SEQ ID NO 35)	:TTTTCGGTGAATCGGATG (SEQ ID NO: 1068)
222	N33 (SEQ ID NO	:TTTTTGGTGAATTGGATG (SEQ ID NO: 1069)
223	N33 (SEQ ID NO	:TGTTATTTCGGAGGGTTT (SEQ ID NO: 1070)
224	N33 (SEQ ID NO	:TGTTATTTTGGAGGGTTT (SEQ ID NO: 1071)
225	P 9	:GTTTAGTTAGCGGGTTTT (SEQ ID NO: 1072)
226		
227	100)	GTTTAGTTAGTGGGTTTT (SEQ ID NO: 1073)
		TTTTTTACGTCGTAGGTAAG (SEQ ID NO: 1074)
228		TTTTTTATGTTGTAGGTAAG (SEQ ID NO: 1075)
229	_1/	ATTTAGTTCGGGGGAGGA (SEQ ID NO: 1076)
230	N33 (SEQ ID NO: 35)	ATTTAGTTTGGGGGAGGA (SEQ ID NO: 1077)
231.	PAX6 (SEQ ID NO: 36)	GAGGGTTATGCGATTTTA (SEQ ID NO: 1078)
232	PAX6 (SEQ ID NO: 36)	GAGGGTTATGTGATTTTA (SEQ ID NO: 1079)
233	PAX6 (SEQ ID	TATTGTTTCGGTTGTTAG (SEQ ID NO: 1080)
234	NO: 36) PAX6 (SEQ ID	TATTGTTTTGGTTGTTAG (SEQ ID NO: 1081)
235	NO: 36) PAX6 (SEQ ID	TTAGTAGCGAGTTTAGGT (SEQ ID NO: 1082)
236	NO: 36) PAX6 (SEQ ID	TTAGTAGTGAGTTTAGGT (SEQ ID NO: 1082)
237	NO: 36) PAX6 (SEQ ID	
238	NO: 36)	GTTTAGGTCGCGTAGATTT (SEQ ID NO: 1084)
239	NO: 36)	GTTTAGGTTGTAGATTT (SEQ ID NO: 1085)
	1.01.30)	AGTTTAGCGTATTTTCGGT (SEQ ID NO: 1086)
40	10.00	AGTTTAGTGTATTTTTTGGT (SEQ ID NO: 1087)
41	X51730 PGR (SEQ ID NO: 67)	TGTATCGAGAGGTTCGATT (SEQ ID NO: 1088)
42		TGTATTGAGAGGTTTGATT (SEQ ID NO: 1089)
43	X51730 PGR	AGGAGTCGCGTGTTATTA (SEQ ID NO: 1090)
	(SEQ ID NO: 67)	· · · · · · · · · · · · · · · · · · ·

244	X51730 PGR (SEQ ID NO: 67)	AGGAGTTGTGTTATTA (SEQ ID NO: 1091)
245	X51730 PGR	
	(SEQ ID NO: 67)	GTTAGGAGACGAGATTTT (SEQ ID NO: 1092)
246	X51730 PGR	<u></u>
	(SEQ ID NO: 67)	GTTAGGAGATGAGATTTT (SEQ ID NO: 1093)
247	X51730 PGR	<u> </u>
2 4 / .		TGTCGTTCGTTGGGATAA (SEQ ID NO: 1094)
240	(SEQ ID NO: 67)	
248	X51730 PGR	TGTTGTTTGGGATAA (SEQ ID NO: 1095)
	(SEQ ID NO: 67)	
249	PTEN (SEQ ID	TTTGCGTTCGTATTTAGAG (SEQ ID NO: 1096)
	NO: 38)	(SEQ ID NO: 1096)
250 _,	PTEN (SEQ ID	TTTGTGTTTCTATTTAGAG
	NO: 38)	TTTGTGTTTTGTATTTAGAG (SEQ ID NO: 1097)
251	PTEN (SEQ ID	<u> </u>
	NO: 38)	TTAGAGTTATCGTTTTGTT (SEQ ID NO: 1098)
252	PTEN (SEQ ID	<u> </u>
	NO: 38)	TTAGAGTTATTGTTTTGTT (SEQ ID NO: 1099)
253		<u> </u>
223	PTEN (SEQ ID	TGATGTGGCGGGATTTTT (SEQ ID NO: 1100)
	NO: 38)	<u> </u>
254	PTEN (SEQ ID	TGATGTGGTGGGATTTTT (SEQ ID NO: 1101)
	NO: 38)	(PEG ID MO: 1101)
255	PTEN (SEQ ID:	TTTTTTCGGAAGTTGTAG (SEQ ID NO: 1102)
	NO: 38)	(SEQ ID NO: 1102)
56	PTEN (SEQ ID	TTTTTTCCAACTTCT
	NO: 38)	TTTTTTTGGAAGTTGTAG (SEQ ID NO: 1103)
57		TA CTA CTTO C C CT
	NO: 39)	TAGTAGTTCGGGTAGGGT (SEQ ID NO: 1104)
58		
	NO: 39)	TAGTAGTTTGGGTAGGGT (SEQ ID NO: 1105)
59		
J 9	RARB (SEQ ID	AGGGTTTATCGAAAGTTT (SEQ ID NO: 1106)
		
60 ·	RARB (SEQ ID	AGGGTTTATTGAAAGTTT (SEQ ID NO: 1107)
		(ppd m Mo. 1107)
61	RARB (SEQ ID	GAGCGATTCGAGTAGGGT (SEQ ID NO: 1108)
		(SEQ ID NO: 1108)
62	RARB (SEQ ID	GAGTGATTTGAGTAGGGT (CDC TT)
	NO: 39)	GAGTGATTTGAGTAGGGT (SEQ ID NO: 1109)
53		GTATCGTCGCCCTAGGAR
	NO: 39)	GTATCGTCGGGGTAGGAT (SEQ ID NO: 1110)
54		
-	NO: 39)	GTATTGTTGGGGTAGGAT (SEQ ID NO: 1111)
55	 	<u> </u>
	RARB (SEQ ID	GAACGTATTCGGAAGGTT (SEQ ID NO: 1112)
· ·		
66	RARB (SEQ ID	GAATGTATTTGGAAGGTT (SEQ ID NO: 1113)
·		•
57 .	SFN (SEQ ID	GAGTAGGTCGAACGTTAT (SEQ ID NO: 1114)
	NO: 40)	(SEQ ID NO: 1114)
8.		GAGTAGGTTGAATGTTAT (SEQ ID NO: 1115)
	NO: 40)	THE STITUTE OF THE SECOND NO. 1115)

269	SFN (SEQ ID NO: 40)	TTTGCGAAGAGCGAAATT (SEQ ID NO: 1116)
270	SFN (SEQ ID NO: 40)	TTTGTGAAGAGTGAAATT (SEQ ID NO: 1117)
271	SFN (SEQ ID NO: 40)	TAACGAGGAGGGTTCGGA (SEQ ID NO: 1118)
272	SFN (SEQ ID NO: 40)	TAATGAGGAGGTTTGGA (SEQ ID NO: 1119)
273	SFN (SEQ ID NO: 40)	GTTCGAGGTGCGTGAGTA (SEQ ID NO: 1120)
274 ·	SFN (SEQ ID NO: 40)	GTTTGAGGTGTGAGTA (SEQ ID NO: 1121)
275	S100A2 (SEQ ID NO: 41)	(SEQ ID NO: 1122)
276		TTTAATTGTGGTTGTGTG (SEQ ID NO: 1123)
277		TATATAGGCGTATGTATG (SEQ ID NO: 1124)
278	S100A2 (SEQ ID NO: 41)	TATATAGGTGTATGTATG (SEQ ID NO: 1125)
279	S100A2 (SEQ ID NO: 41)	TATGTATACGAGTATTGGAT (SEQ ID NO: 1126)
280		TATGTATATGAGTATTGGAT (SEQ ID NO: 1127)
281	S100A2 (SEQ ID NO: 41)	AGTTTTAGCGTGTGTTTA (SEQ ID NO: 1128)
282	S100A2 (SEQ ID NO: 41)	AGTTTTAGTGTGTTTTA (SEQ ID NO: 1129)
283	TFF1 (SEQ ID NO: 42)	TATTTTGGTCGAGGTTTA (SEQ ID NO: 1130)
284	TFF1 (SEQ ID NO: 42)	TATTTTGGTTGAGGTTTA (SEQ ID NO: 1131)
285		AGATAGAGACGTGTATAGT (SEQ ID NO: 1132)
286		AGATAGAGATGTGTATAGT (SEQ ID NO: 1133)
287		TGGTTTTTCGTGAAAGAT (SEQ ID NO: 1134)
88		TGGTTTTTTGTGAAAGAT (SEQ ID NO: 1135)
89		AATATTATCGACGTTTTTT (SEQ ID NO: 1136)
90		ATTATTGATGTTTTTTAGAA (SEQ ID NO: 1137)
91		GAAAACGTGGACGTTTTT (SEQ ID NO: 1138)
92 7	GFBR2 (SEQ ID NO: 43)	GAAAATGTGGATGTTTTT (SEQ ID NO: 1139)
93 7		ATTTGGAGCGAGGAATTT (SEQ ID NO: 1140)

294	TGFBR2 (SEO I	DIATTTCC A CTC A CC
· .		DATTTGGAGTGAGGAATTT (SEQ ID NO: 1141)
295	TGFBR2 (SEQ I	DAGTTGAAAGTCGGTTAAA (SEQ ID NO: 1142)
206		
296	I'GFBR2 (SEQ I	DAGTTGAAAGTTGGTTAAA (SEQ ID NO: 1143)
207		
297	IGFBR2 (SEQ I	DAAAGTTTTCGGAGGGGTT (SEQ ID NO: 1144)
200	F. C. 15)	
298	I GFBR2 (SEQ I	DAAAGTTTTTGGAGGGGTT (SEQ ID NO: 1145)
299		
299	I GFBR2 (SEQ I	DGGTAGTTACGAGAGAGTT (SEQ ID NO: 1146)
300		
1500	I GEBRZ (SEQ II	OGGTAGTTATGAGAGAGTT (SEQ ID NO: 1147)
301		
101	TIMP3 (SEQ ID- NO: 44)	GTTTTCGTTGGAGAAAA (SEQ ID NO: 1148)
302		
207	TIMP3 (SEQ ID NO: 44)	GTTTTTTGTTGGAGAAAA (SEQ ID NO: 1149)
303		
دبرم	TIMP3 (SEQ ID	GAAAATATCGGTATTTTGG (SEQ ID NO: 1150)
304	NO: 44)	
PV4.	TIMP3 (SEQ ID	GAAAATATTGGTATTTTGG (SEQ ID NO: 1151)
305	NO: 44)	
202	TIMP3 (SEQ ID	ATGTGGGGCGCGGGGATA (SEQ ID NO: 1152)
206	NO: 44)	
306	TIMP3 (SEQ ID	ATGTGGGGTGTGGGGATA (SEQ ID NO: 1153)
307	NO: 44)	
70 J.	TIMP3 (SEQ ID NO: 44)	GGGATAAGCGAATTTTTTA (SEQ ID NO: 1154)
308		\perp
	TIMP3 (SEQ ID NO: 44)	GGGATAAGTGAATTTTTTA (SEQ ID NO: 1155)
309		<u> </u>
	VHL (SEQ ID NO: 45)	TATAAGCGTGATGATTGG (SEQ ID NO: 1156)
310	· · · · · · · · · · · · · · · · · · ·	
	VHL (SEQ ID NO: 45)	TATAAGTGTGATGATTGG (SEQ ID NO: 1157)
311	VHL (SEQ ID	
,	NO: 45)	TTTCGTGTGAGATGCGTTA (SEQ ID NO: 1158)
312	VHL (SEQ ID	<u>.</u>
·	NO: 45)	TTTTGTGTGAGATGTGTTA (SEQ ID NO: 1159)
313	VHL (SEQ ID	
	NO: 45)	GAGATGCGTTATTTTCGAA (SEQ ID NO: 1160)
314	VHL (SEQ ID	<u> </u>
,	NO: 45)	GAGATGTGTTATTTTGAA (SEQ ID NO: 1161)
1.5		
,	NO: 45)	TATTGCGCGTTTGATATGA (SEQ ID NO: 1162)
16	L	
~ •	NO: 45)	TATTGTGTTTTGATATGA (SEQ ID NO: 1163)
17		
	ID NO: 46)	ATGAAGAACGGTTAAGGG (SEQ ID NO: 1164)
18.		_
	CDKN1C (SEQ ID NO: 46)	ATGAAGAATGGTTAAGGG (SEQ ID NO: 1165)
	110. 10)	

319	CDKN1C (SEQ ID NO: 46)	TATTTCGAGTTAGGTCGAA (SEQ ID NO: 1166)
320	CDKN1C (SEQ ID NO: 46)	TATTTTGAGTTAGGTTGAA (SEQ ID NO: 1167)
321	CDKN1C (SEQ ID NO: 46)	AATTAGTCGGGGTCGTGA (SEQ ID NO: 1168)
322	CDKN1C (SEQ	AATTAGTTGGGGTTGTGA (SEQ ID NO: 1169)
323	ID NO: 46) CDKN1C (SEQ	TTAGTGTTCGTTTGGAAT (SEQ ID NO: 1170)
324	ID NO: 46) CDKN1C (SEQ	<u> </u>
	ID NO: 46)	TTAGTGTTTGGAAT (SEQ ID NO: 1171)
325	CAV1 (SEQ ID NO: 47)	TAAATATTTCGATTGTTGAT (SEQ ID NO: 1172)
326	CAV1 (SEQ ID NO: 47)	TTTTAAATATTTTGATTGTTG (SEQ ID NO: 1173)
327	CAV1 (SEQ ID NO: 47)	TTGGTATCGTTGAAGAAT (SEQ ID NO: 1174)
328	CAV1 (SEQ ID NO: 47)	TTGGTATTGTTGAAGAAT (SEQ ID NO: 1175)
329	CAV1 (SEQ ID NO: 47)	TAAGACGCGTTTTTTGGA (SEQ ID NO: 1176)
330	CAV1 (SEQ ID NO: 47)	TAAGATGTGTTTTTTGGA (SEQ ID NO: 1177)
331	CAV1 (SEQ ID NO: 47)	AATACGTAGATTCGGAGGT (SEQ ID NO: 1178)
332	CAV1 (SEQ ID NO: 47)	AATATGTAGATTTGGAGGT (SEQ ID NO: 1179)
333	CAV1 (SEQ ID NO: 47)	TAGATTCGGAGGTAGGTA (SEQ ID NO: 1180)
334	CAV1 (SEQ ID NO: 47)	TAGATTTGGAGGTAGGTA (SEQ ID NO: 1181)
335	CDH13 (SEQ ID NO: 48)	TAAAACGAGGGAGCGTTA (SEQ ID NO: 1182)
336	CDH13 (SEQ ID NO: 48)	TAAAATGAGGGAGTGTTA (SEQ ID NO: 1183)
337	CDH13 (SEQ ID NO: 48)	AAGGAATTCGTTTTGTAAA (SEQ ID NO: 1184)
338		· · · · · · · · · · · · · · · · · · ·
339	CDH13 (SEQ ID NO: 48)	AAGTGGTCGTTAGTTTTT (SEQ ID NO: 1186)
340		AAGTGGTTGTTAGTTTTT (SEQ ID NO: 1187)
341		GAGTAGGACGGTGTTAAG (SEQ ID NO: 1188)
342		GAGTAGGATGGTGTTAAG (SEQ ID NO: 1189)
343		TAAATTTAACGTTGGGTAG (SEQ ID NO: 1190)
	NO: 49)	(BEQ ID NO: 1190)

344	NDRG1 (SEQ ID NO: 49)	TAAATTTAATGTTGGGTAG (SEQ ID NO: 1191)
345	NDRG1 (SEQ ID NO: 49)	GATAATGACGGTGTTAGT (SEQ ID NO: 1192)
346	NDRG1 (SEQ ID NO: 49)	(SEQ ID NO: 1193)
347	_ [' ' ' ' ' ' ' ' ' ' ' ' ' ' ' ' ' '	GTTGTACGTTAGGAGTTA (SEQ ID, NO: 1194)
348	NDRG1 (SEQ ID NO: 49)	GTTGTATGTTAGGAGTTA (SEQ ID NO: 1195)
349	PTGS2 (SEQ ID NO: 50)	TTTATCGGGTTTACGTAATT (SEQ ID NO: 1196)
350	PTGS2 (SEQ ID NO: 50)	TTTATTGGGTTTATGTAATT (SEQ ID NO: 1197)
351	PTGS2 (SEQ ID NO: 50)	GTACGAAAAGGCGGAAAG (SEQ ID NO: 1198)
352	PTGS2 (SEQ ID NO: 50)	GTATGAAAAGGTGGAAAG (SEQ ID NO: 1199)
353	PTGS2 (SEQ ID NO: 50)	ATTGGTTTTCGGAAGCGTT (SEQ ID NO: 1200)
354	PTGS2 (SEQ ID NO: 50)	ATTGGTTTTTGGAAGTGTT (SEQ ID NO: 1201)
55	PTGS2 (SEQ ID NO: 50)	AAGCGTTCGGGTAAAGAT (SEQ ID NO: 1202)
56	PTGS2 (SEQ ID NO: 50)	AAGTGTTTGGGTAAAGAT (SEQ ID NO: 1203)
5.7	THBS1 (SEQ ID NO: 51)	TATTTTACGGGGACGGTG (SEQ ID NO: 1204)
58	THBS1 (SEQ ID NO: 51)	TATTTTATGGGGATGGTG (SEQ ID NO: 1205)
59.		GATTAGTTCGTTCGAAAGT (SEQ ID NO: 1206)
60		GATTAGTTTGTTTGAAAGT (SEQ ID NO: 1207)
61	 	GTGGCGTAAGAGTACGAG (SEQ ID NO: 1208)
62	r. O. D. J.	GTGGTGTAAGAGTATGAG (SEQ ID NO: 1209)
63	<u></u>	ATAGGTTACGGGTTGGAG (SEQ ID NO: 1210)
64 	<u></u>	ATAGGTTATGGGTTGGAG (SEQ ID NO: 1211)
	<u></u>	AAATTTGCGAACGTTTGG (SEQ ID NO: 1212)
66 		AAATTTGTGAATGTTTGG (SEQ ID NO: 1213)
57 58		AAATGGAGTTCGTTTTTT (SEQ ID NO: 1214)
	MEFF2 (SEQ ID NO: 52)	AAATGGAGTTTGTTTTTT (SEQ ID NO: 1215)

369	TMEFF2 (SEQ ID NO: 52)	GGTCGATGTTTTCGGTAA (SEQ ID NO: 1216)
370	TMEFF2 (SEQ ID NO: 52)	GGTTGATGTTTTGGTAA (SEQ ID NO: 1217)
371	PLAU (SEQ ID NO: 53)	TGAGGTTTCGTTTTAAGA (SEQ ID NO: 1218)
372	PLAU (SEQ ID NO: 53)	TGAGGTTTTGTTTTAAGA (SEQ ID NO: 1219)
373	PLAU (SEQ ID NO: 53)	TTATTTACGTGTGTGGAG (SEQ ID NO: 1220)
374	PLAU (SEQ ID NO: 53)	TTATTTATGTGTGGAG (SEQ ID NO: 1221)
375	PLAU (SEQ ID NO: 53)	GGTGATTAGCGTTATATATT (SEQ ID NO: 1222)
376	PLAU (SEQ ID NO: 53)	GGTGATTAGTGTTATATATT (SEQ ID NO: 1223)
377	PLAU (SEQ ID NO: 53)	GATAAGTCGTGTTTTGAG (SEQ ID NO: 1224)
378	PLAU (SEQ ID NO: 53)	GATAAGTTGTGTTTTGAG (SEQ ID NO: 1225)
379	μνο. 54)	TAGTTCGTTCGGTGAAGT (SEQ ID NO: 1226)
380	μνυ: 34)	TAGTTTGTTTGGTGAAGT (SEQ ID NO: 1227)
381	μνο. 54)	GTGAAGTTCGTTGTTTTT (SEQ ID NO: 1228)
382	μνΟ: 34)	GTGAAGTTTGTTGTTTTT (SEQ ID NO: 1229)
383	μνΟ. 54)	TTAAACGTTTATCGGTTGG (SEQ ID NO: 1230)
384	/μνΟ. 51 /	TTAAATGTTTATTGGTTGG (SEQ ID NO: 1231)
385	μνο. 54)	TTTAATTTCGTAGAAGAATA (SEQ ID NO: 1232)
386	$\mu \bullet O. J \rightarrow J$	TTTTAATTTTGTAGAAGAATA (SEQ ID NO: 1233)
387	<u>μνο. 54)</u>	GAAGAATACGCGTATTTAGT (SEQ ID NO: 1234)
388	μνο. 54)	GAAGAATATGTGTATTTAGT (SEQ ID NO: 1235)
389	_μνΟ. 33)	GTACGGTGTTCGAGGTAT (SEQ ID NO: 1236)
390	<u> 100. 33)</u>	GTATGGTGTTTGAGGTAT (SEQ ID NO: 1237)
391	$\mu vo. 33)$	TTTTTACGCGGAGTAGTG (SEQ ID NO: 1238)
392	<u>μν</u> Ο. 33)	TTTTTATGTGGAGTAGTG (SEQ ID NO: 1239)
393	DNMT1 (SEQ ID NO: 55)	GGGAATACGTATGCGTAAG (SEQ ID NO: 1240)

394	MO: 22)	GGGAATATGTATGTGTAAG (SEQ ID NO: 1241)
395	INO: 55)	GAACGGAGTCGGTTATGT (SEQ ID NO: 1242)
396	MO: 22)	GAATGGAGTTGGTTATGT (SEQ ID NO: 1243)
397	INO: 55)	AAACGGAGAGAGGCGATA (SEQ ID NO: 1244)
398	DNMT1 (SEQ ID NO: 55)	AAATGGAGAGAGGTGATA (SEQ ID NO: 1245)
399	ESR1 (SEQ ID NO: 70)	TTTTTTGGTCGTGAAATT (SEQ ID NO: 1246)
400 ·	ESR1 (SEQ ID NO: 70)	TTTTTTGGTTGTGAAATT (SEQ ID NO: 1247)
401	ESR1 (SEQ ID NO: 70)	TTTAGTAGCGACGATAAGTA (SEQ ID NO: 1248)
402	ESR1 (SEQ ID NO: 70)	TTTAGTAGTGATAAGTA (SEQ ID NO: 1249)
403	ESR1 (SEQ ID NO: 70)	GGATCGTTTTAAATCGAGT (SEQ ID NO: 1250)
404	ESR1 (SEQ ID NO: 70)	GGATTGTTTTAAATTGAGT (SEQ ID NO: 1251)
405	ESR1 (SEQ ID NO: 70)	TGGAGGTTCGGGAGTTTA (SEQ ID NO: 1252)
406	ESR1 (SEQ ID NO: 70)	TGGAGGTTTGGGAGTTTA (SEQ ID NO: 1253)
407	ESR1 (SEQ ID NO: 70)	TTTTATCGGATTCGTAGGT (SEQ ID NO: 1254)
408	ESR1 (SEQ ID NO: 70)	TTTTATTGGATTTGTAGGT (SEQ ID NO: 1255)
409 .	APAF1 (SEQ ID NO: 57)	AGTAGGACGTGGTCGTTT (SEQ ID NO: 1256)
410	μνο: 37)	AGTAGGATGTGGTTGTTT (SEQ ID NO: 1257)
411	MO: 37) ·	ATTCGGCGGGATTTGATT (SEQ ID NO: 1258)
412	NO: 57)	ATTTGGTGGGATTTGATT (SEQ ID NO: 1259)
413	NO: 37)	TAGCGAGTGGACGTGATT (SEQ ID NO: 1260)
414	APAF1 (SEQ ID NO: 57)	TAGTGAGTGGATGTGATT (SEQ ID NO: 1261)
415	μNO. 38)	AGTTAGTCGGGTTTTAAG (SEQ ID NO: 1262)
416	<u>μνυ: 38)</u>	AGTTAGTTGGGTTTTAAG (SEQ ID NO: 1263)
417	μνΟ: 58)	ATATGGTTTTCGTGTTATT (SEQ ID NO: 1264)
418	HOXA5 (SEQ ID NO: 58)	ATATGGTTTTTGTGTTATT (SEQ ID NO: 1265)

419	HOXA5 (SEQ ID NO: 58)	TTTTTGCGAGCGTATGAG (SEQ ID NO: 1266)
420	<u>μιο. 30)</u>	TTTTTGTGAGTGTATGAG (SEQ ID NO: 1267)
421	μ ₁ Ο. 33)	GTTTCGGGGTTCGTAATA (SEQ ID NO: 1268)
422	μ(Ο. 39)	GTTTTGGGGTTTGTAATA (SEQ ID NO: 1269)
423	, μνο. 33)	AGGTAGTTTTCGAGAATG (SEQ ID NO: 1270)
424	<u></u>	AGGTAGTTTTTGAGAATG (SEQ ID NO: 1271)
425	μ(Ο. 39)	TTTGTGTCGTCGGGAAAT (SEQ ID NO: 1272)
426	μ(O, J) / ·	TTTGTGTTGTTGGGAAAT (SEQ ID NO: 1273)
427		TTAGTTTTCGCGTAGAATTA (SEQ ID NO: 1274)
428 429	μ(Ο, 32)	TTAGTTTTTGTGTAGAATTA (SEQ ID NO: 1275)
430	<u></u>	TATTTGCGGAGTCGGTAA (SEQ ID NO: 1276)
431	_μνο. 39)	TATTTGTGGAGTTGGTAA (SEQ ID NO: 1277)
432	_μνο. 39)	TTTGTAGCGGGTGGAGTA (SEQ ID NO: 1278)
433	μνΟ. 33)	TTTGTAGTGGGTGGAGTA (SEQ ID NO: 1279)
434	$\underline{\mu}$	AAATGCGAATTTCGAGAAA (SEQ ID NO: 1280)
435	_μνο. 1)	AAATGTGAATTTTGAGAAA (SEQ ID NO: 1281)
436	140.1)	TTCGTAGTTTTTCGAGGAA (SEQ ID NO: 1282)
437	NO: 1)	TTTGTAGTTTTTTGAGGAA (SEQ ID NO: 1283)
438	NO: 1)	TAGTTAATTCGGGTCGGG (SEQ ID NO: 1284)
439	NO: 1)	TAGTTAATTTGGGTTGGG (SEQ ID NO: 1285)
440	NO: 1)	TGAGTATAGTCGTTTCGTT (SEQ ID NO: 1286)
441	NO: 1)	TGAGTATAGTTGTTTGTT (SEQ ID NO: 1287)
442	NO: 1)	GTTTATTTGAGTAGTCGTT (SEQ ID NO: 1288)
443	NO: 1)	GTTTATTTGAGTAGTGGTT (SEQ ID NO: 1289)
<u>··</u>	NO: 9)	AATTTTTGCGGTTCGATAG (SEQ ID NO: 1290)

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1		
444	HLA-F (SEQ ID NO: 9)	(BEQ ID NO: 1291)
445	HLA-F (SEQ ID NO: 9)	GGGCGTAGGTTACGATTA (SEQ ID NO: 1292)
446	HLA-F (SEQ ID NO: 9)	GGGTGTAGGTTATGATTA (SEQ ID NO: 1293)
447	HLA-F (SEQ ID NO: 9)	GAGTTTTCGGATTCGAAAT (SEQ ID NO: 1294)
448	HLA-F (SEQ ID NO: 9)	GAGTTTTTGGATTTGAAAT (SEQ ID NO: 1295)
449		GAACGAGGATTTGCGTTT (SEQ ID NO: 1296)
450	HLA-F (SEQ ID NO: 9)	GAATGAGGATTTGTGTTT (SEQ ID NO: 1297)
451		ATTTTAAGGCGTGTTAGT (SEQ ID NO: 1298)
452		ATTTTAAGGTGTGTTAGT (SEQ ID NO: 1299)
453	APOC2 (SEQ ID	
454	NO: 2) APOC2 (SEQ ID	
455	NO: 2) APOC2 (SEQ ID	
456	NO: 2) APOC2 (SEQ ID	TTGGGGGATGTTATTGTT (SEQ ID NO: 1303)
457	NO: 2) APOC2 (SEQ ID	TGGGTTTGCGGAGAATGG (SEQ ID NO: 1304)
458	NO: 2) APOC2 (SEQ ID	TGGGTTTGTGGAGAATGG (SEQ ID NO: 1304)
459		GGTCGAGTCGATAAAGTTT (SEQ ID NO: 1305)
460	ID NO: 3)	GGTTGACTTGATTA
461		GGTTGAGTTGATAAAGTTT (SEQ ID NO: 1307)
462		TTACGTGTTTAAGTACGAAG (SEQ ID NO: 1308)
463		TTATGTGTTTAAGTATGAAG (SEQ ID NO: 1309)
		GAATTGATTCGGGAGTAT (SEQ ID NO: 1310)
464		GAATTGATTTGGGAGTAT (SEQ ID NO: 1311)
465		TAGGTTCGTTTAGAGTTG (SEQ ID NO: 1312)
466	 -/	TAGGTTTGTTTAGAGTTG (SEQ ID NO: 1313)
467	EGR4 (SEQ ID NO: 4)	GGAAGCGTATTTATCGGA (SEQ ID NO: 1314)
468		GGAAGTGTATTTATTGGA (SEQ ID NO: 1315)

469	NO: 4)	(SEQ ID NO: 1316)
470	NO: 4)	AGGTGTAGTGTTTTAGAT (SEQ ID NO: 1317)
471,	EGR4 (SEQ ID NO: 4)	TAACGTTATAGTTCGAGTTT (SEQ ID NO: 1318)
472	EGR4 (SEQ ID NO: 4)	TAATGTTATAGTTTGAGTTT (SEQ ID NO: 1319)
473	AR (SEQ ID NO	: AGAGGTTGCGTTTTAGAG (SEQ ID NO: 1320)
474.	AR (SEQ ID NO	: AGAGGTTGTGTTTTAGAG (SEQ ID NO: 1321)
475	AR (SEQ ID NO	: TTATAGTCGTAGTCGGTTT (SEQ ID NO: 1322)
476	AR (SEQ ID NO	: TTATAGTTGTAGTTGGTTT (SEQ ID NO: 1323)
177	AR (SEQ ID NO	: ITATTTCGAGAGAGGTTG (SEQ ID NO: 1324)
178	AR (SEQ ID NO	: TTATTTTGAGAGAGGTTG (SEQ ID NO: 1325)
179	AR (SEQ ID NO	GTCGTGGTCGTTAGTAAG (SEQ ID NO: 1326)
80	AR (SEQ ID NO	GTTGTGGTTGTTAGTAAG (SEQ ID NO: 1327)
81	AR (SEQ ID NO:	AGTATTTCGGACGAGGA (SEQ ID NO: 1328)
82	AR (SEQ ID NO:	AGTATTTTGGATGAGGA (SEQ ID NO: 1329)
83	RB1 (SEQ ID	-1
84	NO: 6) RB1 (SEQ ID	TATTAGATTTEGGGATAGG (SEQ ID NO: 1330)
85	_NO: 6)	TATTAGATTTTGGGATAGG (SEQ ID NO: 1331)
86	NO: 6) RB1 (SEQ ID	GTAGAAGTACGTTCGGGT (SEQ ID NO: 1332)
37	NO: 6) RB1 (SEQ ID	GTAGAAGTATGTTTGGGT (SEQ ID NO: 1333)
38	NO: 6)	GTATCGATTAGCGTTTTAGT (SEQ ID NO: 1334)
	RB1 (SEQ ID NO: 6)	GTATTGATTAGTGTTTTAGT (SEQ ID NO: 1335)
10 ·	RB1 (SEQ ID NO: 6)	AAAGGCGTTATGTCGTTTA (SEQ ID NO: 1336)
<u>, .</u>		AAAGGTGTTATGTTGTTTA (SEQ ID NO: 1337)
1		TATAAGTTCGCGTTGG (SEQ ID NO: 1338)
2		TTATAAGTTTGTGTTGGT (SEQ ID NO: 1339)
3	BRCA2 (SEQ ID NO: 60)	TATTCGAGGCGTAGTA (SEQ ID NO: 1340)

494	BRCA2 (SEQ ID NO: 60)	TATTTGAGGTGTAGTAGA (SEQ ID NO: 1341)
495	BRCA2 (SEQ ID NO: 60)	TTTATCGTCGTAAAAGAT (SEQ ID NO: 1342)
496 -	BRCA2 (SEQ ID NO: 60)	GATTTATTGTTGTAAAAGAT (SEQ ID NO: 1343)
497	. μ τΟ. Ου)	ATTCGTTTTAGAGGCGTA (SEQ ID NO: 1344)
498	<u> </u>	ATTTGTTTTAGAGGTGTA (SEQ ID NO: 1345)
499	BRCA2 (SEQ ID NO: 60)	TAAGAAGTCGCGGTAG (SEQ ID NO: 1346)
500	BRCA2 (SEQ ID NO: 60)	GTAAGAAGTTGTGGTAG (SEQ ID NO: 1347)
501	μνο. στ)	(BEQ ID NO. 1348)
502	µ\O. 01)	TGTTGGTGTAGTAGTAG (SEQ ID NO: 1349)
503	110.01)	AGAAGCGAGAGTCGAG (SEQ ID NO: 1350)
504	110.01)	TAGAAGTGAGAGTTGAG (SEQ ID NO: 1351)
505	410.01)	TTTTTAACGATCGGGT (SEQ ID NO: 1352)
506	CCND1 (SEQ ID NO: 61)	TTAATGATTGGGTGTTG (SEQ ID NO: 1353)
507	μ40. 01)	TGTCGTTTATGCGGAA (SEQ ID NO: 1354)
508	_μιο. σι)	TGTTGTTTATGTGGAAG (SEQ ID NO: 1355)
509	μ (Ο. ΟΙ)	GGAAGATCGTCGTTAT (SEQ ID NO: 1356)
510	μ (Ο. ΟΙ)	AGATTGTTGTTATTTGGA (SEQ ID NO: 1357)
511	<u></u>	GTTTTATTCGAGAAATGT (SEQ ID NO: 1358)
512	μ (Ο. 02)	TGTTTTATTTGAGAAATGT (SEQ ID NO: 1359)
513	$\mu \cup 0 \cup 0 = 0$	GGAATGTTCGTGTTTTA (SEQ ID NO: 1360)
514	μ10.02)	GGAATGTTTGTGTTTTAT (SEQ ID NO: 1361)
515	F (0 , 02)	TAGGGGTCGATTTTTAA (SEQ ID NO: 1362)
16	<u></u>	TTAGGGGTTGATTTTTAA (SEQ ID NO: 1363)
17	F . C . C _ /	AATATAATCGGTTAGGTTA (SEQ ID NO: 1364)
518	EDNRB (SEQ ID NO: 62)	GATAATATAATTGGTTAGGT (SEQ ID NO: 1365)

519	EGFR (SEQ ID	AAGTTTTCGCGAGTTT (SEQ ID NO: 1366)
•	NO: 63)	<u> </u>
520	EGFR (SEQ ID	AAAGTTTTTGTGAGTTTT (SEQ ID NO: 1367)
	NO: 63)	(520 1201)
521	EGFR (SEQ ID	GTATTATTTCGGACGTT (SEQ ID NO: 1368)
	NO: 63)	(bbQ 1b 140. 1508)
522	EGFR (SEQ ID	TATTTTGGATGTTTGGTA (SEQ ID NO: 1369)
	NO: 63)	1111001111001A (BEQ ID NO: 1369)
523	EGFR (SEQ ID	TTTCGAGAGGGTTTCGTA (SEQ ID NO: 1370)
	NO: 63)	11100NGAGGGTTTCGTA (SEQ ID NO: 1370)
524	EGFR (SEQ ID	TTTTGA GA GGCTTTTGTA (GEO TO NO.
	NO: 63)	TTTTGAGAGGGTTTTGTA (SEQ ID NO: 1371)
525	EGFR (SEQ ID	ATTATTCCACCTTCCT (CEC TO) TO) TO)
· [NO: 63)	ATTATTCGACGTTGGT (SEQ ID NO: 1372)
526	EGFR (SEQ ID	TTATTATTTCATOTTCCT
.	NO: 63)	TTATTATTTGATGTTGGTT (SEQ ID NO: 1373)
527	EGFR (SEQ ID	CTAACTTOCCCCCC + TO CT
727	NO: 63)	GTAAGTTCGCGGGGAT (SEQ ID NO: 1374)
528	EGFR (SEQ ID	OTA A COMPANY
520	NO: 63)	GTAAGTTTGTGGGGAT (SEQ ID NO: 1375)
529		
529	ERBB2 (SEQ ID	AGATCGCGTTATTGTT (SEQ ID NO: 1376)
520	NO: 64)	
530	ERBB2 (SEQ ID	AGAGATTGTGTTATTGTT (SEQ ID NO: 1377)
-	NO: 64)	
531	ERBB2 (SEQ ID	ATTTCGGATTTCGGGGGA (SEQ ID NO: 1378)
	NO: 64)	
532	ERBB2 (SEQ ID	AATTTATTTTGGATTTTGGG (SEQ ID NO: 1379)
	μ+Ο. 0+)	<u>1</u>
533	ERBB2 (SEQ ID	GGATTTTTCGAGGAAAA (SEQ ID NO: 1380)
<u> </u>	NO: 64)	<u> </u>
534	ERBB2 (SEQ ID	GGGATTTTTTGAGGAAA (SEQ ID NO: 1381)
1	NO: 64)	
535	ERBB2 (SEQ ID	TAGGTTTGCGCGAAGA (SEQ ID NO: 1382)
	NO: 64)	(SEQ ID NO. 1382)
536	ERBB2 (SEQ ID	TTTGTGTGAAGAGAGG (SEQ ID NO: 1383)
	NO: 64)	1
537	FOS (SEQ ID	TTTCGGGTTCGAGTAA (SEQ ID NO: 1384)
· ·	NO: 65)	(BEQ ID NO: 1384)
538	FOS (SEQ ID	TTTTGGGTTTGAGTAATA (SEQ ID NO: 1385)
1	NO: 65)	(SEQ ID NO: 1385)
539	FOS (SEQ ID	TTTCGAAGGAATGCGTT (SEQ ID NO: 1386)
1	NO: 65)	(SEQ ID NO: 1386)
540·	FOS (SEQ ID	TTTTGA A GGA A TGTCTT (GDC TO 355
1	NO: 65)	TTTTGAAGGAATGTGTT (SEQ ID NO: 1387)
541	FOS (SEQ ID	AGA A ACGGTATCC A CT (CDC ======
1	NO: 65)	AGAAACGGTATCGAGT (SEQ ID NO: 1388)
542	FOS (SEQ ID	GGA GA A A TCCT A TTG A G
	NO: 65)	GGAGAAATGGTATTGAG (SEQ ID NO: 1389)
543	FOS (SEQ ID	A ATTOTTOGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGG
	NO: 65)	AATTGTTCGCGGGTTGTA (SEQ ID NO: 1390)
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544		AATTGTTTGTGGGTTGTA (SEQ ID NO: 1391)
	NO: 65)	
545	NFKB1 (SEQ IDNO: 66)	TATAGGCGTTCGTTATT (SEQ ID NO: 1392)
516		GGATTATAGGTGTTGTT (SEC. ID NO. 1202)
546	NFKB1 (SEQ ID NO: 66)	GGATTATAGGTGTTTGTT (SEQ ID NO: 1393)
547		TATTACGTTCGGTTAATT (SEQ ID NO: 1394)
5.47	NO: 66)	INTINIOGITOGGITAATT (BEQ ID 140. 1374)
548	NFKB1 (SEQ ID	ATTATGTTTGGTTAATTTTT (SEQ ID NO: 1395)
	NO: 66)	
549	NFKB1 (SEQ ID	AGTTATCGTATTCGGTT (SEQ ID NO: 1396)
	NO: 66)	
550		TGAGTTATTGTATTTGGT (SEQ ID NO: 1397)
	NO: 66)	
551	NFKB1 (SEQ ID	TTTAGTTTTCGGAGTTA (SEQ ID NO: 1398)
1	NO: 66)	
552	NFKB1 (SEO ID	TTAGTTTTTTGGAGTTAAA (SEQ ID NO: 1399)
7	NO: 66)	
553		AAAGGTCGATTGTTGG (SEQ ID NO: 1400)
	NO: 66)	
554		TAAACCTTCATTCCTTCC (SEC ID NO. 1401)
1554		TAAAGGTTGATTGTTGG (SEQ ID NO: 1401)
1	NO: 66)	TI TO COLO LO CONTROL DI COLO
555	X51730 PGR	TATCGAGAGGTTCGAT (SEQ ID NO: 1402)
<u> </u>	(SEQ ID NO: 67)	1
556	X51730 PGR	TGTATTGAGAGGTTTGAT (SEQ ID NO: 1403)
1	(SEQ ID NO: 67)	
557	X51730 PGR	GAGTCGCGTGTTATTA (SEQ ID NO: 1404)
	(SEQ ID NO: 67)	
558	X51730 PGR -	AAAGGAGTTGTGTGTT (SEQ ID NO: 1405)
1	(SEQ ID NO: 67)	
559	X51730 PGR	AAATTGTCGTCGTAGT (SEQ ID NO: 1406)
	(SEQ ID NO: 67)	TAMELITO COLOCIA (BEQ ID NO. 1400)
560	X51730 PGR	ATTAAATTGTTGTTGTAGT (SEQ ID NO: 1407)
Poo	(SEQ ID NO: 67)	
561	X51730 PGR	
561	4 '	TGTCGTTCGTTGGGATAA (SEQ ID NO: 1408)
5.60	(SEQ ID NO: 67)	
562	X51730 PGR	TGTTGTTGGGATAA (SEQ ID NO: 1409)
1	(SEQ ID NO: 67)	
563	TP53 (SEQ ID	TTTTTACGACGGTGAT (SEQ ID NO: 1410)
	NO: 68)	\
564	TP53 (SEQ.ID	TGTTTTTTATGATGGTGA (SEQ ID NO: 1411)
	NO: 68)	
565	TP53 (SEQ ID	GAAAATCGTTGGGGTT (SEQ ID NO: 1412)
	NO: 68)	
566	TP53 (SEQ ID	GGAAAATTGTTGGGGT (SEQ ID NO: 1413)
	NO: 68)	(0.000, 1710)
567		AGTCGGTTTAAAGCGTA (SEQ ID NO: 1414)
. ["	NO: 68)	PLOTOGOTTIANACOTA (SEQ ID NO. 1414)
560		ACTTOOTTTA A A CTOTA TO CORO TO 3 TO 1 44 TO
568	. • • •	AGTTGGTTTAAAGTGTAT (SEQ ID NO: 1415)
· L	NO: 68)	

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569	TP53 (SEQ ID NO: 68)	AGTTTTCGGTTTCGTTAGA (SEQ ID NO: 1416)
570	TP53 (SEQ ID NO: 68)	AGTTTTTGGTTTAGA (SEQ ID NO: 1417)
571	TP73 (SEQ ID NO: 69)	GTGCGAGTTAGTCGGA (SEQ ID NO: 1418)
572	TP73 (SEQ ID NO: 69)	GTGTGAGTTAGTTGGA (SEQ ID NO: 1419)
573	TP73 (SEQ ID NO: 69)	TATCGGTTCGGAGTTA (SEQ ID NO: 1420)
574	TP73 (SEQ ID NO: 69)	AGGATATTGGTTTGGAG (SEQ ID NO: 1421)
575	TP73 (SEQ ID NO: 69)	AGAGTCGTTCGGAATT (SEQ ID NO: 1422)
576	TP73 (SEQ ID NO: 69)	TGAGAGTTGTTTGGAAT (SEQ ID NO: 1423)
577	ESR1 (SEQ ID NO: 70)	TTTTCGCGTTTATTTTAA (SEQ ID NO: 1424)
578	ESR1 (SEQ ID NO: 70)	TTTTTTGTGTTTATTTTAAGT (SEQ ID NO: 1425)
579	ESR1 (SEQ ID NO: 70)	AGTAGATTTTCGTGCGTT (SEQ ID NO: 1426)
580	ESR1 (SEQ ID NO: 70)	AGTAGATTTTGTGTGTT (SEQ ID NO: 1427)
581	ESR1 (SEQ ID NO: 70)	AGTAGCGACGATAAGT (SEQ ID NO; 1428)
582	ESR1 (SEQ ID NO: 70)	TTTAGTAGTGATGATAAGT (SEQ ID NO: 1429)
583,	ESR1 (SEQ ID NO: 70)	GATCGTTTTAAATCGAGT (SEQ ID NO: 1430)
584	ESR1 (SEQ ID NO: 70)	GGATTGTTTTAAATTGAGT (SEQ ID NO: 1431)
585	ESR1 (SEQ ID NO: 70)	TATCGGATTCGTAGGT (SEQ ID NO: 1432)
586	ESR1 (SEQ ID NO: 70)	TTTATTGGATTTGTAGGTT (SEQ ID NO: 1433)
587	SERPINE1 (SEQ ID NO: 71)	AGTCGTGTATTATCGGA (SEQ ID NO: 1434)
588		AGTTGTGTATTATTGGAG (SEQ ID NO: 1435)
589		AGGCGGTCGGGTATAT (SEQ ID NO: 1436)
590		AGGTGGTTGGGTATAT (SEQ ID NO: 1437)
591	<u> </u>	TAGAGTATCGGGTGGA (SEQ ID NO: 1438)
92		AGAGTATTGGGTGGAT (SEQ ID NO: 1439)
593		AGGATATTCGGGAGAG (SEQ ID NO: 1440)
	in MO: 71)	

		·
594		AGGATATTTGGGAGAGA (SEQ ID NO: 1441)
595		TGGCGTTCGTTTTATTAA (SEQ ID NO: 1442)
596	6 CALM1 (SEQ ID NO: 72)	TGGTGTTTGTTTATTAAA (SEQ ID NO: 1443)
597	7 CALMÍ (SEQ ID NO: 72)	AGTAGTATTCGAGTTAAAT (SEQ ID NO: 1444)
598	CALM1 (SEQ ID NO: 72)	AGTAGTATTTGAGTTAAATT (SEQ ID NO: 1445)
599		TAGAGGACGAGGTAGT (SEQ ID NO: 1446)
600		TAGAGGATGAGGTAGTT (SEQ ID NO: 1447)
601	CALM1 (SEQ ID NO: 72)	TTAGTTGTCGAGGAGA (SEQ ID NO: 1448)
602		TTTAGTTGTTGAGGAGA (SEQ ID NO: 1449)
603		TGATTTTCGAATTTTGGT (SEQ ID NO: 1450)
604		TGATTTTTGAATTTTGGT (SEQ ID NO: 1451)
605		GAACGTTTTAGTGCGTT (SEQ ID NO: 1452)
606		GGAATGTTTTAGTGTGTT (SEQ ID NO: 1453)
607	CSNK2B (SEQ	GTGCGAATTAGTTTCGTT (SEQ ID NO: 1454)
608	DOTATED (DEC	GTGTGAATTAGTTTTGTT (SEQ ID NO: 1455)
609	LAST WATER (DEG	ATTTTCGGTTAATTCGTT (SEQ ID NO: 1456)
610	CSNK2B (SEQ	ATTTTTGGTTAATTTGTTG (SEQ ID NO: 1457)
611	FGFR1 (SEQ ID	GTATTTCGTTGGTTAAGT (SEQ ID NO: 1458)
612	FGFR1 (SEQ ID	GTGTATTTGTTGGTTAA (SEQ ID NO: 1459)
613	FGFR1 (SEQ ID	ATGTGAACGAAGTTAAG (SEQ ID NO: 1460)
614	NO: 74) FGFR1 (SEQ ID	ATGTGAATGAAGTTAAGA (SEQ ID NO: 1461)
615	NO: 74)	FATGTTTCGGGGAAGT (SEQ ID NO: 1461)
516	NO: 74)	
517	NO: 74)	TATGTTTTGGGGAAGTA (SEQ ID NO: 1463)
518	NO: 74)	TATGATTCGTTTTTTAAGA (SEQ ID NO: 1464)
5	NO: 74)	AGTTATGATTTGTTTTTAA (SEQ ID NO: 1465)

	•	•
619	MKI67 (SEQ ID NO: 75)	TTGAGATCGCGTTATT (SEQ ID NO: 1466)
620	MKI67 (SEQ ID NO: 75)	AGTTGAGATTGTGTTATT (SEQ ID NO: 1467)
621	MKI67 (SEQ ID NO: 75)	AGGATCGTTTGAGTCGGG (SEQ ID NO: 1468)
622	MKI67 (SEQ ID NO: 75)	AGGATTGTTTGAGTTGGG (SEQ ID NO: 1469)
623	MKI67 (SEQ ID NO: 75)	AAATTCGTTAGGCGTG (SEQ ID NO: 1470)
624	MKI67 (SEQ ID NO: 75)	AATTTGTTAGGTGTGGT (SEQ ID NO: 1471)
625	MKI67 (SEQ ID NO: 75)	TGAGTTCGGGAGTTTA (SEQ ID NO: 1472)
626	MKI67 (SEQ ID NO: 75)	TTGAGTTTGGGAGTTTA (SEQ ID NO: 1473)
627	NPM1 (SEQ ID NO: 76)	AGTAGTATTCGTTTATTTT (SEQ ID NO: 1474)
628	NPM1 (SEQ ID NO: 76)	GAGTAGTATTTGTTTATTTT (SEQ ID NO: 1475)
629	NPM1 (SEQ ID NO: 76)	ATTTAAGTGCGTGTTGT (SEQ ID NO: 1476)
530	NPM1 (SEQ ID NO: 76)	ATTTAAGTGTGTGTTGT (SEQ ID NO: 1477)
631	NPM1 (SEQ ID NO: 76)	GTTTTTCGATGGAAGAT (SEQ ID NO: 1478)
632	NPM1 (SEQ ID NO: 76)	TGTTTTTTGATGGAAGAT (SEQ ID NO: 1479)
533	NPM1 (SEQ ID NO: 76)	TGATGGACGTGGATAT (SEQ ID NO: 1480)
634	NPM1 (SEQ ID NO: 76)	TTGATGGATGTGGATAT (SEQ ID NO: 1481)
	' μνΟ. //)	AGTTTTACGTTTCGATT (SEQ ID NO: 1482)
536		TGTAGTTTTATGTTTTGAT (SEQ ID NO: 1483)
537	_pxO. //j	AAGAAACGATCGAATTT (SEQ JD NO: 1484)
38 39	μιο. //)	AAATGATTGAATTTGGGA (SEQ ID NO: 1485)
540	<u>μιο. 77)</u>	ATTTATTTTCGTGTGTAT (SEQ ID NO: 1486)
41	<u> </u>	AATTTATTTTTTGTGTGTAT (SEQ ID NO: 1487)
42	μτΟ. ///	GTGTATCGTGTTTTTAAT (SEQ ID NO: 1488)
43 :	2.0.77	TGTGTATTGTGTTTTTAAT (SEQ ID NO: 1489)
, CT	SYK (SEQ ID NO: 78)	GAAGTTATCGCGTTGG (SEQ ID NO: 1490)

644	SYK (SEQ ID NO: 78)	AGAAGTTATTGTGTTGG (SEQ ID NO: 1491)
645	SYK (SEQ ID NO: 78)	GATCGATGCGGTTTAT (SEQ ID NO: 1492)
646	SYK (SEQ ID NO: 78)	GGGATTGATGTGGTTTA (SEQ ID NO: 1493)
647	SYK (SEQ ID NO: 78)	GTTCGGCGGGAGGAGA (SEQ ID NO: 1494)
648	SYK (SEQ ID NO: 78)	GTTTGGTGGGAGGAGA (SEQ ID NO: 1495)
649	SYK (SEQ ID NO: 78)	AGTCGATTTCGTTTAG (SEQ ID NO: 1496)
650	SYK (SEQ ID NO: 78)	TAGTTGATTTTGTTTAGT (SEQ ID NO: 1497)
651	SYK (SEQ ID NO: 78)	GGAAGAGTCGCGGGTT (SEQ ID NO: 1498)
652	SYK (SEQ ID NO: 78)	GGAAGAGTTGTGGGTT (SEQ ID NO: 1499)
653	TK2 (SEQ ID NO: 79)	AAGTTTCGAGTGTGAT (SEQ ID NO: 1500)
654	TK2 (SEQ ID NO: 79)	AAGTTTTGAGTGTGATG (SEQ ID NO: 1501)
655	TK2 (SEQ ID NO: 79)	TTAAGACGGTGGAGAT (SEQ ID NO: 1502)
656	TK2 (SEQ ID NO: 79)	TTTTAAGATGGTGGAGA (SEQ ID NO: 1503)
657	TK2 (SEQ ID NO: 79)	GAATTACGGTGATGGT (SEQ ID NO: 1504)
658	TK2 (SEQ ID NO: 79)	GAATGAATTATGGTGATG (SEQ ID NO: 1505)
659	TK2 (SEQ ID NO: 79)	AGGTAATTGTCGATTAGA (SEQ ID NO: 1506)
660	TK2 (SEQ ID NO: 79)	AGGTAATTGTTGATTAGAT (SEQ ID NO: 1507)
661	TK2 (SEQ ID NO: 79)	GTGTGTTTTCGTAAATA (SEQ ID NO: 1508)
662	TK2 (SEQ ID NO: 79)	GTGTGTTTTTGTAAATAA (SEQ ID NO: 1509)
663	HSPB1 (SEQ ID NO: 80)	GTGTTACGGTAGGGTA (SEQ ID NO: 1510)
664	HSPB1 (SEQ ID NO: 80)	GTGTTATGGTAGGGTAT (SEQ ID NO: 1511)
665	HSPB1 (SEQ ID NO: 80)	AGTCGTGTTACGGTAG (SEQ ID NO: 1512)
666	HSPB1 (SEQ ID NO: 80)	AGTTGTGTTATGGTAGG (SEQ ID NO: 1513)
667	HSPB1 (SEQ ID NO: 80)	TTTTTCGTTAAGGAAAG (SEQ ID NO: 1514)
668 ,	HSPB1 (SEQ ID NO: 80)	TTTTTTTTTTAAGGAAAG (SEQ ID NO: 1515)

669	TES (SEQ ID NO: 81)	TAGAAGTCGGTTCGTG (SEQ ID NO: 1516)
670	TES (SEQ ID NO: 81)	AGAAGTTGGTTTGTGG (SEQ ID NO: 1517)
671	TES (SEQ ID NO: 81)	GTTCGTGGACGTTTAGA (SEQ ID NO: 1518)
672	TES (SEQ ID NO: 81)	GTTTGTGGATGTTTAGA (SEQ ID NO: 1519)
673	TES (SEQ ID NO: 81)	GATTGGGCGGCGGAAG (SEQ ID NO: 1520)
674.	TES (SEQ ID NO: 81)	ATTGGGTGGAAGT (SEQ ID NO: 1521)
675	TES (SEQ ID NO: 81)	TAGCGGAGTCGGAGGT (SEQ ID NO: 1522)
676	TES (SEQ ID NO: 81)	TAGTGGAGTTGGAGGT (SEQ ID NO: 1523)
677	TES (SEQ ID NO: 81)	AATTCGGTCGTGGGAT (SEQ ID NO: 1524)
678	TES (SEQ ID NO: 81)	AATTTGGTTGTGGGAT (SEQ ID NO: 1525)
6.79	SDC4 (SEQ ID NO: 82).	TTGCGGGTTATACGAT (SEQ ID NO: 1526)
680	SDC4 (SEQ ID NO: 82)	TTTGTGGGTTATATGATT (SEQ ID NO: 1527)
681	SDC4 (SEQ ID NO: 82)	GTGAATCGTGTTAAGAT (SEQ ID NO: 1528)
682	SDC4 (SEQ ID NO: 82)	TGTGAATTGTGTTAAGAT (SEQ ID NO: 1529)
683	PITX2 (SEQ ID NO: 83)	AGTCGGGAGAGCGAAA (SEQ ID NO: 1838)
684	PITX2 (SEQ ID NO: 83)	AGTTGGGAGAGTGAAA (SEQ ID NO: 1839)
685 _.	PITX2 (SEQ ID NO: 83)	AAGAGTCGGGAGTCGGA (SEQ ID NO: 1840)
686	PITX2 (SEQ ID NO: 83)	AAGAGTTGGGAGTTGGA (SEQ ID NO: 1841)
687 ·	PITX2 (SEQ ID NO: 83)	GGTCGAAGAGTCGGGA (SEQ ID NO: 1842)
688	PITX2 (SEQ ID NO: 83)	GGTTGAAGAGTTGGGA (SEQ ID NO: 1843)
689	PITX2 (SEQ ID NO: 83)	ATGTTAGCGGGTCGAA (SEQ ID NO: 1530)
690	PITX2 (SEQ ID NO: 83)	TAGTGGGTTGAAGAGT (SEQ ID NO: 1531)
591	GPR37 (SEQ ID NO: 84)	TTTCGATAGCGTTTGA (SEQ ID NO: 1532)
592	GPR37 (SEQ ID NO: 84)	TTTTGATAGTGTTTGATTT (SEQ ID NO: 1533)
593	GPR37 (SEQ ID . NO: 84)	ATAGCGGAAGATCGGT (SEQ ID NO: 1534)

694	GPR37 (SEQ ID NO: 84)	ATAGTGGAAGATTGGTT (SEQ ID NO: 1535)
695	GPR37 (SEQ ID NO: 84)	TAGCGGGGAATCGGAG (SEQ ID NO: 1536)
696	GPR37 (SEQ ID NO: 84)	TAGTGGGGAATTGGAG (SEQ ID NO: 1537)
697	GPR37 (SEQ ID NO: 84)	ATTTATTTCGTTCGGGTA (SEQ ID NO: 1538)
698	GPR37 (SEQ ID NO: 84)	ATTTATTTTGTTTGGGTA (SEQ ID NO: 1539)
699	GPR37 (SEQ ID NO: 84)	ATTCGGTAGTCGTAGT (SEQ ID NO: 1540)
700	GPR37 (SEQ ID , NO: 84)	ATTTGGTAGTTGTAGTTT (SEQ ID NO: 1541)
701	FGF1 (SEQ ID NO: 85)	TATAGGTTCGCGGATT (SEQ ID NO: 1542)
702	FGF1 (SEQ ID NO: 85)	TTATAGGTTTGTGGATTG (SEQ ID NO: 1543)
703	FGF1 (SEQ ID NO: 85)	ATTATTCGGGAATTTTGT (SEQ ID NO: 1544)
704	FGF1 (SEQ ID NO: 85)	TATTATTTGGGAATTTTGT (SEQ ID NO: 1545)
705	FGF1 (SEQ ID NO: 85)	AGTTTTGATCGAGAAGT (SEQ ID NO: 1546)
706	FGF1 (SEQ ID NO: 85)	TAGTTTTGATTGAGAAGT (SEQ ID NO: 1547)
707	FGF1 (SEQ ID NO: 85)	TAGTAACGGGGTTAT (SEQ ID NO: 1548)
709	FGF1 (SEQ ID NO: 85)	TGTAGTAATGGGGGTT (SEQ ID NO: 1549)
710	FGF1 (SEQ ID NO: 85)	GATTTTTCGGATGGTA (SEQ ID NO: 1550)
711	FGF1 (SEQ ID NO: 85)	ATTTTTTGGATGGTATAG (SEQ ID NO: 1551)
712	μνΟ: δΟ)	GAGAGTCGGGATGATT (SEQ ID NO: 1552)
713	μνΟ: δο)	GGAGAGTTGGGATGAT (SEQ ID NO: 1553)
714	μνΟ. δυ)	AGAGACTTCGATTTGGA (SEQ ID NO: 1554)
715	_μνΟ. δυ)	AAGAGATTTTGATTTGGA (SEQ ID NO: 1555)
716	_μνΟ: δο)	TAGGGTCGAGATTTGG (SEQ ID NO: 1556)
717	μνΟ. δΟ)	TTAGGGTTGAGATTTGG (SEQ ID NO: 1557)
	μνο. ου)	AGTGTGGCGAATATTG (SEQ ID NO: 1558)
718	GRIN2D (SEQ ID NO: 86)	GTGTGGTGAATATTGAA (SEQ ID NO: 1559)

719	CTSB (SEQ ID	TGGGATATTCGAGGAAT (SEQ ID NO: 1560)
	NO: 87)	SEQ ID NO: 1560)
720	CTSB (SEQ ID	GGATATTTGAGGAATTGA (SEQ ID NO: 1561)
701	NO: 87)	*
721	CTSB (SEQ ID	TGATATGCGTTATGGTT (SEQ ID NO: 1562)
722	NO: 87)	
	CTSB (SEQ ID NO: 87)	TTGATATGTTTATGGTT (SEQ ID NO: 1563)
723	CTSD (SEQ ID	TAGAGGCGAGCGGTA (SEQ ID NO: 1564)
	NO: 88)	122726 GCGAGCGGTA (SEQ ID NO: 1564)
724	CTSD (SEQ ID	TAGAGGGTGAGTGGTA (SEQ ID NO: 1565)
	NO: 88)	<u></u>
725	CTSD (SEQ ID	GGAGCGCGAAAGTTAT (SEQ ID NO: 1566)
726	NO: 88)	
/26	CTSD (SEQ ID	TAGGGGAGTGTGAAAG (SEQ ID NO: 1567)
727	NO: 88) CTSD (SEQ ID	TACCACOTOGO COTO
12/	NO: 88)	TAGGAGGTCGCGTAGG (SEQ ID NO: 1568)
728	CTSD (SEQ ID	TAGGAGGTTCTCTAGG (GTO TO
	NO: 88)	TAGGAGGTTGTGTAGG (SEQ ID NO: 1569)
729	CTSD (SEQ ID	ATTCGTTTAGATTCGGG (SEQ ID NO: 1570)
<u> </u>	NO: 88)	(SEQ ID NO: 1570)
730	CTSD (SEQ ID	ATTTGTTTAGATTTGGGG (SEQ ID NO: 1571)
	NO: 88)	(BEQ ID 1(0. 15/1)
731	PLAUR (SEQ ID	GGTATAGCGGGAAGT (SEQ ID NO; 1572)
700	NO: 89)	
732	PLAUR (SEQ ID	GGTATAGTGGGAAGTAA (SEQ ID NO: 1573)
733	NO: 89)	1
733	NO: 89)	ATTTATATTTATCGTTAAAGT (SEQ ID NO: 1574)
734	PLAUR (SEO ID	TATATTTATTGTTAAAGTTTTT (SEQ ID NO: 1575)
	NO: 89)	(SEQ ID NO: 1575)
735	PLAUR (SEQ ID	AGAGCGATTGTTTCGGG (SEQ ID NO: 1576)
	μ10. 02.)	
736	PLAUR (SEQ ID	AGAGTGATTGTTTTGGG (SEQ ID NO: 1577)
727	μνΟ. 89)	
737	PLAUR (SEQ ID	GGGTTTTACGTTAGGA (SEQ ID NO: 1578)
738	NO: 89) PLAUR (SEQ ID	
	NO: 89)	GGGTTTTATGTTAGGAA (SEQ ID NO: 1579)
739	PSA (SEQ ID	TTTCGATTCGGTTTAGA (GEO TO NO. 100 ii
L	NO: 90)	TTTCGATTCGGTTTAGA (SEQ ID NO: 1824)
740	PSA (SEQ ID	AATTGTTTTGATTTGGTT (SEQ ID NO: 1825)
	NO: 90)	
741	PSA (SEQ ID	TAATGGGGCGTCGATT (SEQ ID NO: 1826)
740	NO: 90)	
742	PSA (SEQ ID	TTAATGGGGTGTTGATT (SEQ ID NO: 1827)
743	NO: 90)	
د ۳۰	PSA (SEQ ID NO: 90)	TATCGTAGCGGTTAGG (SEQ ID NO: 1828)
	μτΟ, 90)	

744	PSA (SEQ ID NO: 90)	TATTGTAGTGGTTAGGAA (SEQ ID NO: 1829)
745	PSA (SEQ ID NO: 90)	AGGAACGTTAGTCGTT (SEQ ID NO: 1830)
746	PSA (SEQ ID NO: 90)	TAGGAATGTTAGTTGTTT (SEQ ID NO: 1831)
747	PSA (SEQ ID NO: 90)	GGTCGTCGTATTATGGA (SEQ ID NO: 1832)
748	PSA (SEQ ID NO: 90)	TGGTTGTTGTATTATGGA (SEQ ID NO: 1833)
749	CGA (SEQ ID NO: 91)	ATATTTATTTTCGGAAATTT (SEQ ID NO: 1580)
750	CGA (SEQ ID NO: 91)	TTATTTTTGGAAATTTATAGT (SEQ ID NO: 1581)
751.	CGA (SEQ ID NO: 91)	TGATTTTGTCGTTATTATT (SEQ ID NO: 1582)
752	CGA (SEQ ID NO: 91)	TTGATTTGTTGTTATTATT (SEQ ID NO: 1583)
753 .	CGA (SEQ ID NO: 91)	TAAATTGACGTTATGGTA (SEQ ID NO: 1834)
7.54	CGA (SEQ ID NO: 91)	AAATTGATGTTATGGTAAA (SEQ ID NO: 1835)
755	CGA (SEQ ID NO: 91)	AATTGACGTTATGGTAAT (SEQ ID NO: 1836)
756	CGA (SEQ ID NO: 91)	TAAAAATTGATGTTATGGT (SEQ ID NO: 1837)
757	μNO: 92)	AAGTAGCGGTAAGGAT (SEQ ID NO: 1584)
758	μνυ: 92)	GAAGTAGTGGTAAGGAT (SEQ ID NO: 1585)
759	μNO: 92)	TAGAGGGCGAAGGTTA (SEQ ID NO: 1586)
760	μNO: 92)	AGAGGGTGAAGGTTAT (SEQ ID NO: 1587)
761	μνΟ. 323	TGTATCGGTATTAACGTT (SEQ ID NO: 1588)
762 	μνω. 32)	TGTATTGGTATTAATGTTG (SEQ ID NO: 1589)
763	μNO: 92)	GTACGTTATTCGTTAGG (SEQ ID NO: 1590)
764	_μνΟ. 92)	TGTATGTTATTTGTTAGGT (SEQ ID NO: 1591)
765 766	μνΟ. 93)	AAAAGAGTCGTATAGAGA (SEQ ID NO: 1592)
766 - 767	μνο. 93)	AAGAGTTGTATAGAGAGG (SEQ ID NO: 1593)
767 768	_ μ(Ο. 93)	GTGTGTCGGGAGTTATA (SEQ ID NO: 1594)
	NO: 93)	GTGTGTTGGGAGTTATA (SEQ ID NO: 1595)

769	CYP3A4 (SEQ ID NO: 93)	AAATAGGCGATGTTTAA (SEQ ID NO: 1596)
770	μNO: 93)	TAGAAATAGGTGATGTTT (SEQ ID NO: 1597)
771	μνω: 93)	TAAAATTATAGCGTTTTTAA (SEQ ID NO: 1598)
772	μιο. 93)	AAATTATAGTGTTTTTAAAAT (SEQ ID NO: 1599)
773	TK1 (SEQ ID NO: 94)	AGGAATTCGGTACGTG (SEQ ID NO: 1600)
774	TK1 (SEQ ID NO: 94)	GAGGAATTTGGTATGTG (SEQ ID NO: 1601)
775	TK1 (SEQ ID NO: 94)	AATTACGAGTCGGTTT (SEQ ID NO: 1602)
776	TK1 (SEQ ID NO: 94)	GGTTAATTATGAGTTGGT (SEQ ID NO: 1603)
777	TK1 (SEQ ID NO: 94)	AGGTCGTTTCGTAGTA (SEQ ID NO: 1604)
778	TK1 (SEQ ID NO: 94)	TTAAGGTTGTTTTGTAGT (SEQ ID NO: 1605)
779	TK1 (SEQ ID NO: 94)	TTTCGGGAAGTTTACGAA (SEQ ID NO: 1606)
780	TK1 (SEQ ID NO: 94)	TTTTGGGAAGTTTATGAA (SEQ ID NO: 1607)
781	RENBP (SEQ ID NO: 95)	TAGATTTTCGGTTATTTT (SEQ ID NO: 1608)
782	RENBP (SEQ ID NO: 95)	TTTAGATTTTTGGTTATTT (SEQ ID NO: 1609)
783	μιο: 95)	GGTTTATTCGAGTGGA (SEQ ID NO: 1610)
784	<u>μνΟ: 93)</u> .	TGGTTTATTTGAGTGGA (SEQ ID NO: 1611)
785	μνο. 33)	TAAAGTTTCGTTTTAGGT (SEQ ID NO: 1612)
786	μνο: 93),	TTAAAGTTTTGTTTTAGGT (SEQ ID NO: 1613)
787	INO: 95)	GGGATCGCGATTAATT (SEQ ID NO: 1614)
788	μνο: 93)	GGGATTGTGATTAATTTTG (SEQ ID NO: 1615)
789	(0 0)	TGGATTAACGGACGGA (SEQ ID NO: 1616)
790	190)	TTGGATTAATGGATGGA (SEQ ID NO: 1617)
791	190)	GGACGGACGTTATGAG (SEQ ID NO: 1618)
792	1701	GGATGGATGTTATGAGG (SEQ ID NO: 1619)
793	F12 (SEQ ID NO: 96)	ATATTTCGGTGAGTGT (SEQ ID NO: 1620)

794	F12 (SEQ ID NO: 96)	AATATTTTTGGTGAGTGT (SEQ ID NO: 1621)
795		GGGGGGTCGTTATTATA (SEQ ID NO: 1622)
796		GGGGGGTTGTTATTATA (SEQ ID NO: 1623)
797	F12 (SEQ ID NO: 96)	GTTAGTTCGGAAGGTT (SEQ ID NO: 1624)
798		GGTTAGTTTGGAAGGT (SEQ ID NO: 1625)
99	RÉN (SEQ ID NO: 97)	TTATTGCGGGATAGAG (SEQ ID NO: 1626)
300	REN (SEQ ID NO: 97)	TTATTGTGGGATAGAGT (SEQ ID NO: 1627)
801	REN (SEQ ID NO: 97)	TTTTTAGCGAGGTATTT (SEQ ID NO: 1628)
302	REN (SEQ ID NO: 97)	AGTTTTTAGTGAGGTATT (SEQ ID NO: 1629)
303	REN (SEQ ID NO: 97)	GTTTGTCGGGAGATTA (SEQ ID NO: 1630)
304	REN (SEQ ID NO: 97)	TGTTTGTTGGGAGATTA (SEQ ID NO: 1631)
305	REN (SEQ ID NO: 97)	TAATTATCGTTTAAAGGTG (SEQ ID NO: 1632)
306	REN (SEQ ID NO: 97)	TTAATTATTGTTTAAAGGTG (SEQ ID NO: 1633)
307	EBAG9 (SEQ ID NO: 98)	GTTTGACGTCGAGATT (SEQ ID NO: 1634)
308	EBAG9 (SEQ ID NO: 98)	TGATGTTGAGATTGGG (SEQ ID NO: 1635)
309	EBAG9 (SEQ ID NO: 98)	TTATCGGGAAATTCGTT (SEQ ID NO: 1636)
310		ITTTATTGGGAAATTTGTT (SEQ ID NO: 1637)
311	EBAG9 (SEQ ID NO: 98)	ATTTTTAGTTTCGTTTATTT (SEQ ID NO: 1638)
312	EBAG9 (SEQ ID NO: 98)	TTTAGTTTTGTTTATTTAAAG (SEQ ID NO: 1639)
313	MSMB (SEQ ID NO: 99)	ATTGGTATCGTTGAGG (SEQ ID NO: 1640)
814	MSMB (SEQ ID NO: 99)	ATTGGTATTGTTGAGGT (SEQ ID NO: 1641)
315	MSMB (SEQ ID NO: 99)	TGTATAAAATCGAATAAGG (SEQ ID NO: 1642)
16	MSMB (SEQ ID NO: 99)	TGTATAAAATTGAATAAGGA (SEQ ID NO: 1643)
17		ATAGGGCGAAGGTTTA (SEQ ID NO: 1644)
		ATAGGGTGAAGGTTTAG (SEQ ID NO: 1645)

819	X15323	TAGTTTCGGGAGATGT (SEQ ID NO: 1646)
	angiotensinogen	
	gene 5'-region and	·
	exon 1 (SEQ ID	
<u></u>	NO: 100)	
820	X15323	TTAGTTTTGGGAGATGT (SEQ ID NO: 1647)
· ·	angiotensinogen	
•	gene 5'-region and	
1	exon 1 (SEQ ID	
	NO: 100)	
821	X15323	TAGGAGTCGGGGTTAA (SEQ ID NO: 1648)
	angiotensinogen	
l i	gene 5'-region and	
	exon 1 (SEQ ID	
Ĺ	NO: 100)	
822	X15323	TAGGAGTTGGGGTTAA (SEQ ID NO: 1649)
1	angiotensinogen	(550 10 10 10 10 10 10 10 10 10 10 10 10 10
	gene 5'-region and	
) '	exon 1 (SEQ ID	
	NO: 100)	
823	X15323	AGTGAGTCGGTGTAGG (SEQ ID NO: 1650)
	angiotensinogen	rio Toro Totalo (SEQ ID No. 1650)
ļ	gene 5'-region and	
1	exon 1 (SEQ ID	
-	NO: 100)	
824	X15323	GACTGACTTCCTCTAC (SEC. ID NO. 1651)
102	angiotensinogen	GAGTGAGTTGGTGTAG (SEQ ID NO: 1651)
	gene 5'-region and	
	exon 1 (SEQ ID	
1 .	NO: 100)	
825	X15323	GAAGGGATATTTA GGTT (GPO ID NO. 1650)
023	angiotensinogen	GAAGCGATATTTACGTT (SEQ ID NO: 1652)
	gene 5'-region and	
<u> </u>	exon 1 (SEQ ID	
	NO: 100)	
826		A CA A COTO A MA TOMMA TO THE TOTAL TOTAL TO THE TOTAL TO THE TOTAL TO THE TOTAL TO THE TOTAL TO THE TOTAL TO THE TOTAL TO THE TOTAL TO THE TOTAL TO THE TOTAL TO THE TOTAL TO THE TOTAL TO THE TOTAL TO THE TOTAL TO THE TOTAL TO THE TOTAL TO THE TOTAL TO THE TOTAL TO THE TOTAL TO THE TOTAL TO
020	X15323	AGAAGTGATATTTATGTTG (SEQ ID NO: 1653)
	angiotensinogen	
1	gene 5'-region and	
į	exon 1 (SEQ ID	
007	NO: 100)	
827	ZNF147 (SEQ ID	TAGGTAACGTATAGAGAT (SEQ ID NO: 1654)
200	NO: 101)	
828	ZNF147 (SEQ ID	TTTAGGTAATGTATAGAGA (SEQ ID NO: 1655)
<u></u>	NO: 101)	
829	ZNF147 (SEQ ID	AGGAGTGTCGTATTTTA (SEQ ID NO: 1656)
	NO: 101)	
830	ZNF147 (SEQ ID	AGGAGTGTTGTATTTTAG (SEQ ID NO: 1657)
<u></u>	NO: 101)	
831	ZNF147 (SEQ ID	AGGTTAGCGATTTTGA (SEQ ID NO: 1658)
	NO: 101)	
832		AGGTTAGTGATTTTGAG (SEQ ID NO: 1659)
		1 140. 1033)

1		
	NO: 101)	
833	EBBP (SEQ ID NO: 102)	TTTAGGTCGTTTTTATTTAT (SEQ ID NO: 1660)
834	EBBP (SEQ ID NO: 102)	TTTAGGTTGTTTTATTTATA (SEQ ID NO: 1661)
835	EBBP (SEQ ID NO: 102)	ATGGTATCGAGTCGTT (SEQ ID NO: 1662)
836	EBBP (SEQ ID NO: 102)	TGGTATTGAGTTGTTTAT (SEQ ID NO: 1663)
837	EBBP (SEQ ID NO: 102)	GGAATGTTTCGTTAAGT (SEQ ID NO: 1664)
838	EBBP (SEQ ID NO: 102)	ATGTTTTGTTAAGTGGG (SEQ ID NO: 1665)
839	EBBP (SEQ ID NO: 102)	TTACGAGTGTGACGGA (SEQ ID NO: 1666)
840	EBBP (SEQ ID NO: 102)	TTATGAGTGTGATGGAT (SEQ ID NO: 1667)
841	CALR (SEQ ID NO: 103)	TGTTTTTACGTTGTAGAA (SEQ ID NO: 1668)
842	CALR (SEQ ID NO: 103)	GTTTTTATGTTGTAGAAAG (SEQ ID NO: 1669)
843	CALR (SEQ ID NO: 103)	AGAGGTACGTGATTGG (SEQ ID NO: 1670)
844	CALR (SEQ ID NO: 103)	TAGAGGTATGTGATTGG (SEQ ID NO: 1671)
845	CALR (SEQ ID NO: 103)	TTTTTTAATCGGTAAATGA (SEQ ID NO: 1672)
846	CALR (SEQ ID NO: 103)	TTTTTTAATTGGTAAATGAA (SEQ ID NO: 1673)
847	CALR (SEQ ID NO: 103)	AGATTGTAGTCGTTTTTT (SEQ ID NO: 1674)
848	CALR (SEQ ID NO: 103)	AGATTGTAGTTGTTTTTT (SEQ ID NO: 1675)
849	CALR (SEQ ID NO: 103)	AGGTTTAACGATGTGAT (SEQ ID NO: 1676)
850	CALR (SEQ ID NO: 103)	AGGTTTAATGATGTGATT (SEQ ID NO: 1677)
851	BCAR1 (SEQ ID NO: 104)	AGTTTTCGATTTAGCGTT (SEQ ID NO: 1678)
852 -	BCAR1 (SEQ ID NO: 104)	AGTTTTTGATTTAGTGTTT (SEQ ID NO: 1679)
853 [.]	BCAR1 (SEQ ID NO: 104)	TGGCGAGTTTTCGATTTA (SEQ ID NO: 1680)
854	BCAR1 (SEQ ID NO: 104)	TGGTGAGTTTTTGATTTA (SEQ ID NO: 1681)
855	BCAR1 (SEQ ID NO: 104)	TTTCGATTGTAGACGGT (SEQ ID NO: 1682)
856	BCAR1 (SEQ ID NO: 104)	TTTTGATTGTAGATGGTT (SEQ ID NO: 1683)
857	BCAR1 (SEQ ID	ATTTATCGCGTGTTTAT (SEQ ID NO: 1684)

1	NO: 104)	1
858		GGTATTTATTGTGTGTTTA (SEQ ID NO: 1685)
	NO: 104)	
859		TTGTTCGAAGATCGTT (SEQ ID NO: 1686)
	ID NO: 105)	11011001110011 (bbQ ib ito: 1000)
860		GTTGTTTGAAGATTGTTT (SEQ ID NO: 1687)
000	ID NO: 105)	OTTOTTTOAAGATTOTTT (SEQ ID NO. 1087)
861		TA COOTA A CO ATTOOCT (OF O TO MO. 1 (00)
861		TAGCGTAAGGATTCGGT (SEQ ID NO: 1688)
0.60	ID NO: 105)	
862		TTAGTGTAAGGATTTGGT (SEQ ID NO: 1689)
<u> </u>	ID NO: 105)	
863		AGAGTTCGGTTTTTCGTA (SEQ ID NO: 1690)
<u> </u>	ID NO: 105)	
864	COX7A2L (SEQ	AGAGTTTGGTTTTTGTA (SEQ ID NO: 1691)
L	ID NO: 105)	
865	COX7A2L (SEQ	ATTCGTATTTGCGGGTTA (SEQ ID NO: 1692)
	ID NO: 105)	
866	COX7A2L (SEQ.	ATTTGTATTTGTGGGTTA (SEQ ID NO: 1693)
	ID NO: 105)	
867	AF174646	GTTCGTATAGCGTAGAT (SEQ ID NO: 1694)
1	glandular	,
1.	kallikrein gene,	
1	promoter region	
	and partial	
] '	sequence (SEQ ID	
	NO: 106)	
868	AF174646	GTTTGTATAGTGTAGATGT (SEQ ID NO: 1695)
	glandular	(620 25 1.0. 10,5)
- '	kallikrein gene,	
1	promoter region	
	and partial	
ì	sequence (SEQ ID	
, }	NO: 106)	
869	AF174646	AGAGGCGCGTTGTAGG (SEQ ID NO: 1696)
	glandular	richiddededi i diridd (bbQ ib No. 1090)
	kallikrein gene,	
ļ ·	promoter region	
Į.	and partial	
· .	sequence (SEQ II	
	NO: 106)	
870	AF174646	A CA COTOTOTA CO (SEO ID NO. 1607)
1870	glandular	AGAGGTGTTGTAGG (SEQ ID NO: 1697)
·]	kallikrein gene,	
-	promoter region	
	and partial	
1	sequence (SEQ II	7
071	NO: 106)	Tring Co. I compate co. Co.
871	AF174646	TTGGGACGTGACGGGA (SEQ ID NO: 1698)
İ	glandular kallikrein gene,	
I .		

1	L	1
1	promoter region	
	and partial	
	sequence (SEQ ID NO: 106)	1
872	AF174646	TTGGGATGTGATGGGA (GEO ID NO. 1600)
	glandular	TTGGGATGTGATGGGA (SEQ ID NO: 1699)
}	kallikrein gene,	
	promoter region	
1. ⋅	and partial	
1	sequence (SEQ ID	
	NO: 106)	
873	AF174646	TAGGGGACGTACGTTT (SEQ ID NO: 1700)
	glandular	MOGGACGIACGIII (SEQID NO: 1700)
	kallikrein gene,	
\ ,	promoter region	
1 .	and partial	
J	sequence (SEQ ID	
)	NO: 106)	
874	AF174646	TATTAGGGGATGTATGTT (SEQ ID NO: 1701)
	glandular	THE TAGGGGATGTATGTT (SEQ ID NO: 1/01)
ł · ·	kallikrein gene,	
f	promoter region	
.]	and partial	
}. :	sequence (SEQ ID	
1	NO: 106)	
875	KLK3 (SEQ ID	AATCGGGGATCGTATT (SEQ ID NO: 1702)
	NO: 107)	LATICOGONAL COTATT (SEQ ID NO: 1702)
876	KLK3 (SEQ ID	AGA ATTGGGGATTGTAT (GEO ID NO. 1500)
13	NO: 107)	AGAATTGGGGATTGTAT (SEQ ID NO: 1703)
877	KLK3 (SEQ ID	ATTTGTATTCGGAGAGT (SEQ ID NO: 1704)
1 .	NO: 107)	(SEQ ID NO: 1704)
878	KLK3 (SEQ ID	TGTATTTGGAGAGTTGT (SEQ ID NO: 1705)
	NO: 107)	131A11100A0A01101 (SEQ ID NO: 1/05)
879		GTTTCGCGTGGTAGAA (SEQ ID NO: 1706)
1	ID NO: 108)	STITEGEG TOGTAGAA (SEQ ID NO: 1/06)
880	AKR1B1 (SEQ	GTTTTGTGTGGTAGAAA (GDO TO) 10 1505)
	ID NO: 108)	GTTTTGTGTGGTAGAAA (SEQ ID NO: 1707)
881		GTTGCGCGAAGGACTT (GDO TD NO 1700)
	ID NO: 108)	GTTGCGCGAAGGAGTT (SEQ ID NO: 1708)
882		GTTGTGTGA A GC A GTT (GEO YP) 10 170)
	ID NO: 108)	GTTGTGTGAAGGAGTT (SEQ ID NO: 1709)
883		AGTTCGTGA GGTCCCTA (GFC TD) C 4510
	ID NO: 108)	AGTTCGTGAGGTCGGTA (SEQ ID NO: 1710)
884		A GTTTGTG A CGTTGGT A (GDG TD)
-	ID NO: 108)	AGTTTGTGAGGTTGGTA (SEQ ID NO: 1711)
885		ATTTTOCTTT ACTA COOR (C-
	ID NO: 108)	ATTITCGTTTAGTACGGT (SEQ ID NO: 1712)
886		CATTTTOTTTA CTLATA
المرات	ID NO: 108)	GATTTTTGTTTAGTATGGT (SEQ ID NO: 1713)
887		TAATAAAATTTOOGAA
	1- OTHE (BECK ID	TAATAAAATTTCGGAATTTT (SEQ ID NO: 1714)

	NO: 109)	
888	TGM4 (SEQ ID NO: 109)	TAATAAAATTTTGGAATTTTT (SEQ ID NO: 1715)
389		GGAAGGCGATGTTGAT (SEQ ID NO: 1716)
390	TGM4 (SEQ ID NO: 109)	GGAAGGTGATGTTGAT (SEQ ID NO: 1717)
891	TGM4 (SEQ ID NO: 109)	ATATAGTCGGTTTTTAGG (SEQ ID NO: 1718)
892	TGM4 (SEQ ID NO: 109)	TATAGTTGGTTTTTAGGG (SEQ ID NO: 1719)
893	TGM4 (SEQ ID NO: 109)	AGGTATTCGGTAGAGG (SEQ ID NO: 1720)
894	TGM4 (SEQ ID NO: 109)	AGGTATTTGGTAGAGGT (SEQ ID NO: 1721)
895 ·		AAGAGGCGAAAAGTAG (SEQ ID NO: 1722)
896	AR (SEQ ID NO: 110)	AAGAGGTGAAAAGTAGT (SEQ ID NO: 1723)
897	AR (SEQ ID NO: 110)	AGTAAGCGGTTGTATAT (SEQ ID NO: 1724)
898	AR (SEQ ID NO:	AAAAGTAAGTGGTTGTAT (SEQ ID NO: 1725)
899		AAATTGAGCGTTTATGT (SEQ ID NO: 1726)
900		ATTGAGTGTTATGTGTA (SEQ ID,NO: 1727)
901	HSPA1A (SEQ ID NO: 111)	AGGCGTCGGGAGATTA (SEQ ID NO: 1728)
902	HSPA1A (SEQ ID NO: 111)	AGGTGTTGGGAGATTA (SEQ ID NO: 1729)
903	HSPA1A (SEQ ID NO: 111)	TTGCGTAATTTGGACGTT (SEQ ID NO: 1730)
904	HSPA1A (SEQ ID NO: 111)	TTGTGTAATTTGGATGTT (SEQ ID NO: 1731)
905	HSPA1A (SEQ ID NO: 111)	GTTCGGTTACGTTATAAT (SEQ ID NO: 1732)
906	HSPA1A (SEQ ID NO: 111)	GTTTGGTTATGTTATAATGG (SEQ ID NO: 1733)
907	HSPA1A (SEQ ID NO: 111)	TTGATATCGTTCGGTTA (SEQ ID NO: 1734)
908	HSPA1A (SEQ ID NO: 111)	TGTTGATATTGTTTGGTTA (SEQ ID NO::1735)
909	HSPA1A (SEQ ID NO: 111)	ATGGCGATGTTGATCGTT (SEQ ID NO: 1736)
910	HSPA1A (SEQ ID NO: 111)	ATGGTGATGTTGATTGTT (SEQ ID NO: 1737)
91.1	FKBP4 (SEQ ID NO: 112)	TTTATATTTCGTCGTAGG (SEQ ID NO: 1738)
912	FKBP4 (SEQ ID	TTTTTATATTTTGTTGTAGG (SEQ ID NO: 1739)

	NO: 112)	1
913		ATGTCGGGAGATCGAT (SEQ ID NO: 1740)
914	FKBP4 (SEQ ID NO: 112)	GATGTTGGGAGATTGAT (SEQ ID NO: 1741)
915	FKBP4 (SEQ ID NO: 112)	AGGTCGTCGGGGAGAT (SEQ ID NO: 1742)
916	FKBP4 (SEQ ID NO: 112)	AGGTTGTTGGGGAGAT (SEQ ID NO: 1743)
917	FKBP4 (SEQ ID NO: 112)	AGATTTCGAGTTCGAG (SEQ ID NO: 1744)
918	FKBP4 (SEQ ID NO: 112)	ATTTTGAGTTTGAGGGT (SEQ ID NO: 1745)
919	ESR2 (SEQ ID NO: 113)	ATTTCGAGGATTACGTT (SEQ ID NO: 1746)
920	ESR2 (SEQ ID NO: 113)	ATTTTGAGGATTATGTTTT (SEQ ID NO: 1747)
921	ESR2 (SEQ ID NO: 113)	AGATGGCGTTTTTCGTA (SEQ ID NO: 1748)
922	ESR2 (SEQ ID NO: 113)	TAGATGGTGTTTTTTGTA (SEQ ID NO: 1749)
923	ESR2 (SEQ ID NO: 113)	ATTTTCGAATCGATTTTT (SEQ ID NO: 1750)
924	ESR2 (SEQ ID NO: 113)	GGAGTATTTTGAATTGAT (SEQ ID NO: 1751)
925	ESR2 (SEQ ID NO: 113)	AGTTCGACGGTTTTAG (SEQ ID NO: 1752)
926	ESR2 (SEQ ID NO: 113)	AGGGAGTTTGATGGTT (SEQ ID NO: 1753)
927	ESR2 (SEQ ID NO: 113)	AGTTTACGTGATCGAG (SEQ ID NO: 1754)
928	ESR2 (SEQ ID NO: 113)	AGTTTATGTGATTGAGTT (SEQ ID NO: 1755)
929	IGF1 (SEQ ID NO: 114)	AGATTATGTCGAGTTGT (SEQ ID NO: 1756)
930	IGF1 (SEQ ID NO: 114)	AAGATTATGTTGAGTTGT (SEQ ID NO: 1757)
931	IGF1 (SEQ ID NO: 114)	TAGTATTCGGGTGATTT (SEQ ID NO: 1758)
932	IGF1 (SEQ ID NO: 114)	AGATAGTATTTGGGTGAT (SEQ ID NO: 1759)
933	IGF1 (SEQ ID NO: 114)	AGAAAGGACGATAAGAT (SEQ ID NO: 1760)
934	IGF1 (SEQ ID NO: 114)	AGAAAGGATGATAAGATT (SEQ ID NO: 1761)
935	VTN (SEQ ID NO: 115)	GGTGGTATCGATTGAT (SEQ ID NO: 1762)
936.	VTN (SEQ ID NO: 115)	TGGTGGTATTGATTGAT (SEQ ID NO: 1763)
937	VTN (SEQ ID	TAGTGATTCGCGGGGA (SEQ ID NO: 1764)

!

þ	NO: 115)	
8	VTN (SEQ ID	TAGTGATTTGTGGGGA (SEQ ID NO: 1765)
	NO: 115)	
	VTN (SEQ ID	TTATGTCGGAGGATGA (SEQ ID NO: 1766)
	NO: 115)	
	VTN (SEQ ID	ATTATGTTGGAGGATGA (SEQ ID NO: 1767)
	NO: 115)	
	VTN (SEQ ID	ATACGGTTTATGACGAT (SEQ ID NO: 1768)
	NO: 115)	
12	VTN (SEQ ID	ATATGGTTTATGATGATGG (SEQ ID NO: 1769)
	NO: 115)	
43	CTSL (SEQ ID	GGGTCGGGTGGACGAA (SEQ ID NO: 1770)
	NO: 116)	
44	CTSL (SEQ ID	GGGTTGGGTGGATGAA (SEQ ID NO: 1771)
• •	NO: 116)	
45	CTSL (SEQ ID	TAAACGTGGGGTCGGG (SEQ ID NO: 1772)
	NO: 116)	
46.	CTSL (SEQ ID	TAAATGTGGGGTTGGG (SEQ ID NO: 1773)
-tU '	NO: 116)	
47	CTSL (SEQ ID	GAGCGTTCGAGTTAAT (SEQ ID NO: 1774)
'	NO: 116)	Gracorrodictivity
48	CTSL (SEQ ID	TTGGAGTGTTTGAGTTA (SEQ ID NO: 1775)
40		TIGOAGIGITIGAGITA (BBQ IB No. 1773)
140	NO: 116)	AGGACGAAGAAGCGGA (SEQ ID NO: 1776)
949	1	AGGACGAAGAGCGGA (SEQ ID NO. 1770)
250	NO: 117)	A CO'A TO A A C A A CTCC A (SEO ID NO. 1777)
950.	TGFB3 (SEQ ID	AGGATGAAGAAGTGGA (SEQ ID NO: 1777)
	NO: 117)	THE COLUMN COMPANY (OFFICE ID NO. 1779)
951	TGFB3 (SEQ ID	TAGGAAGCGTTGGTAA (SEQ ID NO: 1778)
<u></u> ;	NO: 117)	TOTAL COLLA COMPANIO COLLA (CITAL TO NO. 1770)
952	TGFB3 (SEQ ID	TTTAGGAAGTGTTGGTA (SEQ ID NO: 1779)
	NO: 117)	
953 .	TGFB3 (SEQ ID	TAGTAGACGTGTAGAAG (SEQ ID NO: 1780)
	NO: 117)	
954		AGTAGATGTGTAGAAGG (SEQ ID NO: 1781)
	NO: 117)	
955	TGFB3 (SEQ II	AGGTTGATCGTGGTAA (SEQ ID NO: 1782)
<u>.</u>	NO: 117)	
956	TGFB3 (SEQ II	AGGTTGATTGTGGTAAA (SEQ ID NO: 1783)
	NO: 117)	
957	MAPKAPK5	AGTAGTCGTTTTTCGGGA (SEQ ID NO: 1784)
	(SEQ ID NO:	
	118)	
958	MAPKAPK5	AGTAGTTGTTTTTGGGA (SEQ ID NO: 1785)
	(SEQ ID NO:	
'	118)	
959	MAPKAPK5	AATTCGGTAGTCGATG (SEQ ID NO: 1786)
'	(SEQ ID NO:	
1	118)	
960	MAPKAPK5	ATTTGGTAGTTGATGGA (SEQ ID NO: 1787)
	(SEQ ID NO:	
	<u></u>	

..

ŀ	118)	
	MAPKAPK5	ATTCGGGGGAGGTCGAA (SEQ ID NO: 1788)
T - [(SEQ ID NO:	
	118)	
	MAPKAPK5	ATTTGGGGGAGGTTGAA (SEQ ID NO: 1789)
02	(SEQ ID NO:	
·	` '	
	118)	ATTTACGGAATTCGGG (SEQ ID NO: 1790)
63	MAPKAPK5	ATTIACOGAATICOGO (BEQ 15 No. 1770)
	(SEQ ID NO:	
	118)	
964	MAPKAPK5	TTATGGAATTTGGGGG (SEQ ID NO: 1791)
	(SEQ ID NO:	
	118)	
965	PCAF (SEQ ID	GAGCGGTAGGTGTCGAA (SEQ ID NO: 1792)
	NO: 119)	
966	PCAF (SEQ ID	GAGTGGTAGGTGTTGAA (SEQ ID NO: 1793)
, 50	NO: 119)	
067	PCAF (SEQ ID	TAAGATTTCGCGGGTA (SEQ ID NO: 1794)
967	•	IMIGHT I COCCOUNTY (DDQ ID 110. 117.)
0.50	NO: 119)	TGTAAGATTTTGTGGGTA (SEQ ID NO: 1795)
968	PCAF (SEQ ID	IGIAAGAITIIGIGGGIA (SEQID NO. 1795)
	NO: 119)	
969	PCAF (SEQ ID	AGTTCGTAGTTTCGAG (SEQ ID NO: 1796)
	NO: 119)	
970	PCAF (SEQ ID	GTTTGTAGTTTTGAGGA (SEQ ID NO: 1797)
	NO: 119)	
971	PCAF (SEQ ID	TAGGGCGCGGAGTAGA (SEQ ID NO: 1798)
1	NO: 119)	
972	PCAF (SEQ ID	TAGGGTGTGGAGTAGA (SEQ ID NO: 1799)
3/2	NO: 119)	
0772	NO. 119).	D GATGATATTTCGGGATTA (SEQ ID NO: 1800)
973		D GAIGAIAI I ICOGGAI IA (BEQ ID NO. 1000)
	NO: 120)	DIGATICATION TO A TEXT OF COLOR AND A COLO
974		D GATGATATTTTGGGATTAA (SEQ ID NO: 1801)
	NO: 120)	
975		D ATAGTTTCGTGGTTTTCGAT (SEQ ID NO: 1802)
1.	NO: 120)	
976	NCOA3 (SEQ.)	D ATAGTTTTGTGGTTTTTGAT (SEQ ID NO: 1803)
1	NO: 120)	
977	NCOA3 (SEO	ID TTTAGTTCGTTTATTTGAA (SEQ ID NO: 1804)
[''	NO: 120)	
978	NCOA3 (SEO	ID TTTAGTTTGTTTATTTGAAA (SEQ ID NO: 1805)
7/8	NO: 120)	
070	NICO 42 (CD)	ID AGGATTCGTGTTTGGTA (SEQ ID NO: 1806)
979		IN MODEL LOCATION LOCATION HOUSE
-	NO: 120)	ID A COA TITTO OTA (GEO ID NO. 1907)
, 980		ID AGGATTTGTGTTTGGTA (SEQ ID NO: 1807)
<u> </u>	NO: 120)	
981	PRKCD (SEQ	ID ATTTATTTTCGTTGTAGG (SEQ ID NO: 1808)
-{	NO: 121)	
982	PRKCD (SEO	ID TATTTATTTTTTGTTGTAGG (SEQ ID NO: 1809)
· [NO: 121)	
		ID TTTCGGAAACGGGAAT (SEQ ID NO: 1810)

	NO: 121)	
984	JNO: 121)	TAGTTTTGGAAATGGGA (SEQ ID NO: 1811)
985	μνο: 121)	GGACGGAGTTATCGGT (SEQ ID NO: 1812)
986	μνυ: 121)	GGATGGAGTTATTGGTA (SEQ ID NO: 1813)
987	μνυ: 121)	GTTTAGCGGAGGGATA (SEQ ID NO: 1814)
988.	PRKCD (SEQ ID NO: 121)	TGTTTAGTGGAGGGAT (SEQ ID NO: 1815)

Table 3: Hybridisation oligonucleotides according to Examples 3 and 4.

No:	Gene	Oligo:
1	STMN1 (SEQ ID	GTTATCGGTTCGGGAATT (SEQ ID NO: 1816)
	NO: 27)	,
2	STMN1 (SEQ ID	GTTATTGGTTTGGGAATT (SEQ ID NO: 1817)
1	NO: 27)	
β	STMN1 (SEQ ID	GTTATCGGTTCGGGAATT (SEQ ID NO: 1816)
4	NO: 27)	
 	STMN1 (SEQ ID	GTTATTGGTTTGGGAATT (SEQ ID NO: 1817)
5	NO: 27)	
β.	STMN1 (SEQ ID NO: 27)	GTAAGAACGTATATAGTGAG (SEQ ID NO:
6		[1818]
	STMN1 (SEQ ID NO: 27)	GTAAGAATGTATATAGTGAG (SEQ ID NO:
7	STMN1 (SEQ ID	1819)
√,	NO: 27)	GTAAGAACGTATATAGTGAG (SEQ ID NO:
8	STMN1 (SEQ ID	1818)
	NO: 27)	GTAAGAATGTATATAGTGAG (SEQ ID NO: 1819)
9	STMN1 (SEQ ID	<u> </u>
	NO: 27)	AGAAATTACGATGATGTTAT (SEQ ID NO: 1820)
10	STMN1 (SEQ ID	AGAAATTATGATGATGTTAT (SEQ ID NO:
	NO: 27)	1821)
11	STMN1 (SEQ ID	AGAAATTACGATGATGTTAT (SEQ ID NO:
	NO: 27)	[1820]
12	STMN1 (SEQ ID	AGAAATTATGATGATGTTAT (SEQ ID NO:
	NO: 27)	[1821]
13	STMN1 (SEQ ID	ATGGGTGATACGTCGGTG (SEQ ID NO:
1.4	NO: 27)	[1822]
14	STMN1 (SEQ ID	ATGGGTGATATGTTGGTG (SEQ ID NO: 1823)
15	NO: 27)	
12	STMN1 (SEQ ID NO: 27)	ATGGGTGATACGTCGGTG (SEQ ID NO:
16		[1822]
	STMN1 (SEQ ID NO: 27)	ATGGGTGATATGTTGGTG (SEQ ID NO: 1823)
17	PSA (SEQ ID NO:	<u>l </u>
	90)	TTTCGATTCGGTTTAGA (SEQ ID NO: 1824)
18	PSA (SEQ ID NO:	
	TENT (BEQ ID NO:	AATTGTTTTGATTTGGTT (SEQ ID NO: 1825)

•

·	90)	1
.9	PSA (SEQ ID NO:	TAATGGGGCGTCGATT (SEQ ID NO: 1826),
	90)	
20	PSA (SEQ ID NO:	TTAATGGGGTGTTGATT (SEQ ID NO: 1827)
,	90)	
21	PSA (SEQ ID NO:	TATCGTAGCGGTTAGG (SEQ ID NO: 1828)
	90)	
22	PSA (SEQ ID NO:	TATTGTAGTGGTTAGGAA (SEQ ID NO: 1829)
	90)	
23	PSA (SEQ ID NO:	AGGAACGTTAGTCGTT (SEQ ID NO: 1830)
•	90)	
24 .	PSA (SEQ ID NO:	TAGGAATGTTAGTTGTTT (SEQ ID NO: 1831)
	90)	
25 ·	PSA (SEQ ID NO:	GGTCGTCGTATTATGGA (SEQ ID NO: 1832)
	90)	, , , , , , , , , , , , , , , , , , , ,
26	PSA (SEQ ID NO:	TGGTTGTTGTATTATGGA (SEQ ID NO: 1833)
T T	90)	
27	CGA (SEQ ID NO:	TAAATTGACGTTATGGTA (SEQ ID NO: 1834)
- 7.	91)	111111111111111111111111111111111111111
28.	CGA (SEQ ID NO:	AAATTGATGTTATGGTAAA (SEQ ID NO:
20,	91)	1835)
29	CGA (SEQ ID NO:	
	91)	AATTOACGTTATOGTAAT (BEQ ID NO. 1830)
30	CGA (SEQ ID NO:	TAAAAATTGATGTTATGGT (SEQ ID NO:
50	91)	1837)
31		_
) i	PITX2 (SEQ ID	AGTCGGGAGAGCGAAA (SEQ ID NO: 1838)
20	NO: 83)	ACTTOCO A CA CTO A A COTO ID NO 1020)
32	PITX2 (SEQ ID	AGTTGGGAGAGTGAAA (SEQ ID NO: 1839)
· · · · ·	NO: 83)	LOTOGOGA GA GOGA A A (GTO TO NO. 1000)
33	PITX2 (SEQ ID	AGTCGGGAGAGCGAAA (SEQ ID NO: 1838)
24	NO: 83)	A COTTOGG A CA COTTO A A A COTTO TO MIC. 1020)
34	PITX2 (SEQ ID	AGTTGGGAGAGTGAAA (SEQ ID NO: 1839)
-	NO: 83)	LA CA CITACIONAL COMO CONTRATA
35	PITX2 (SEQ ID	AAGAGTCGGAGTCGGA (SEQ ID NO: 1840)
	NO: 83)	
36	PITX2 (SEQ ID	AAGAGTTGGGAGTTGGA (SEQ ID NO: 1841)
	NO: 83)	
37	PITX2 (SEQ ID	AAGAGTCGGGAGTCGGA (SEQ ID NO: 1840)
,	NO: 83)	
38 :	PITX2 (SEQ ID	AAGAGTTGGGAGTTGGA (SEQ ID NO: 1841)
	NO: 83)	
39	PITX2 (SEQ ID	GGTCGAAGAGTCGGGA (SEQ ID NO: 1842)
•	NO: 83)	(
40	PITX2 (SEQ ID	GGTTGAAGAGTTGGGA (SEQ ID NO: 1843)
	NO: 83)	
41 ' "	PITX2 (SEQ ID	GGTCGAAGAGTCGGGA (SEQ ID NO: 1842)
,	NO: 83)	
42	PITX2 (SEQ ID	GGTTGAAGAGTTGGGA (SEQ ID NO: 1843)
•	NO: 83)	

Claims

1. A method for predicting the responsiveness of a subject with a cell proliferative disorder of the breast tissues to a therapy comprising one or more drugs which target the estrogen receptor pathway or are involved in estrogen metabolism, production, or secretion, said method comprising analysing the methylation pattern of a target nucleic acid comprising one or a combination of the genes taken from the group consisting of PITX 2, CGA, PSA, and STMN land/or their regulatory regions by contacting at least one of said target nucleic acids in a biological sample obtained from said subject prior to or during treatment with the above mentioned substances.

A method according to Claim 1, wherein said target nucleic acid or acids comprise essentially one or more sequences from the group consisting of SEQ ID Nos: 27, 90, 91 and 83 and sequences complementary thereto.

- 3. A method according to Claims 1 or 2, wherein said cell proliferative disorder of the breast tissue is selected from the group consisting of ductal carcinoma in situ, lobular carcinoma, colloid carcinoma, tubular carcinoma, medullary carcinoma, metaplastic carcinoma, intraductal carcinoma in situ, lobular carcinoma in situ and papillary carcinoma in situ.
- 4. A method according to Claim 3, wherein said subjects are estrogen and/or progesterone receptor positive.
- 5. A method according to Claims 1 to 4, wherein said endocrine therapy is an adjuvant treatment.
- 6. A method according to Claims 5 or 6, wherein the target nucleic acid comprises the gene PITX 2 and/or its regulatory region.
- 7. A method according to Claims 1 to 4, wherein said endocrine therapy is for the treatment of a relapse or metastatic cell proliferative disorder of the breast tissues.
- 8. A method according to claim 7, wherein said subjects have received chemotherapy.

- 9. A method according to claim 8 wherein the genes are selected from the group comprising STMN 1 and PSA.
- 10. A method according to claim 7, wherein said subjects did not receive chemotherapy.
- 11. A method according to claim 8 wherein the genes are selected from the group comprising CGA, STMN 1, and PSA.
- A nucleic acid molecule consisting essentially of a sequence at least 18 bases in length according to one of the sequences taken from the group consisting of SEQ ID Nos: 188, 189, 430, 431, 314-317, 556 to 559, 300, 301, 542 and 543 and sequences complementary thereto.
- An oligomer, in particular an oligonucleotide or peptide nucleic acid (PNA)-oligomer, said oligomer consisting essentially of at least one base sequence having a length of at least 10 nucleotides which hybridises to or is identical to one of the nucleic acid sequences according to SEQ ID NO: 188, 189, 430, 431, 314 to 317, 556 to 559, 300, 301, 542 and 543.
- 14. The oligomer as recited in Claim 13, wherein the base sequence includes at least one CpG dinucleotide.
- 15. The oligomer as recited in Claim 14, characterised in that the cytosine of the CpG dinucleotide is located approximately in the middle third of the oligomer.
- 16. A set of oligomers, comprising at least two oligomers according to any of claims 13 to 15.
- 17. A set of oligomers as recited in Claim 16, comprising oligomers for detecting the methylation state of all CpG dinucleotides within the group of SEQ ID NO: 188, 189, 430, 431, 314 to 317, 556 to 559, 300, 301, 542 and 543 and sequences complementary thereto.

- 18. A set of at least two oligonucleotides as recited in one of Claims 13 through 17, which is used as primer oligonucleotides for the amplification of nucleic acid sequences of one of SEQ ID NO: 188, 189, 430, 431, 314 to 317, 556 to 559, 300, 301, 542 and 543 and sequences complementary thereto.
- 19. A set of oligonucleotides as recited in one of Claims 16 through 12, characterised in that at least one oligonucleotide is bound to a solid phase.
- Use of a set of oligonucleotides comprising at least three of the oligomers according to any of claims 13 through 19 for detecting the cytosine methylation state and/or single nucleotide polymorphisms (SNPs) within the sequences taken from the group SEQ ID Nos: 188, 189, 430, 431, 314 to 317, 556 to 559, 300, 301, 542 and 543 and sequences complementary thereto.
- 21. A method for manufacturing an arrangement of different oligomers (array) fixed to a carrier material for predicting breast cell proliferative disorders' response to tamoxifen treatment by analysis of the methylation state of any of the CpG dinucleotides of the group SEQ ID Nos: 188, 189, 430, 431, 314 to 317, 556 to 559, 300, 301, 542 and 543, wherein at least one oligomer according to any of the claims 13 through 19 is coupled to a solid phase.
- 22. An arrangement of different oligomers (array) obtainable according to claim 21.
- 23. An array of different oligonucleotide- and/or PNA-oligomer sequences as recited in Claim 22, characterised in that said oligonucleotides are arranged on a plane solid phase in the form of a rectangular or hexagonal lattice.
- 24. The array as recited in any of the Claims 22 or 23, characterised in that the solid phase surface is composed of silicon, glass, polystyrene, aluminium, steel, iron, copper, nickel, silver, or gold.
- 25. A DNA- and/or PNA-array for predicting breast cell proliferative disorders' response to tamoxifen treatment by analysis of the methylation state of any of the CpG dinucleotides of the group SEQ ID Nos: 188, 189, 430, 431, 314 to 317, 556 to 559,

300, 301, 542 and 543 comprising at least one nucleic acid according to one of the preceding claims.

- 26. A method according to any one of Claims 1 to 3 comprising the following steps: a)obtaining a biological sample containing genomic DNA,
 - b) extracting the genomic DNA,
 - c) converting cytosine bases in the genomic DNA sample which are unmethylated at the 5-position, to uracil or another base which is dissimilar to cytosine in terms of base pairing behavior;
 - d) amplifying at least one fragment of the pretreated genomic DNA, wherein said fragments comprise one or more sequences selected from the group consisting of SEQ ID NO: 188, 189, 430, 431, 314 to 317, 556 to 559, 300, 301, 542 and 543 and regulatory regions thereof, and sequences complementary thereto, and
 - e) determining the methylation status of one or more genomic CpG dinucleotides by analysis of the amplificate nucleic acids.
- The method according to Claim 26, characterised in that Step e) is carried out by means of hybridisation of at least one oligonucleotide according to SEQ ID NO: 1816, 1816, 1817, 1817, 1818, 1818, 1819, 1819, 1820, 1820, 1821, 1821, 1822, 1822, 1823, 1823 to 1838, 1838, 1839, 1839, 1840, 1840, 1841, 1841, 1842, 1842, 1843, and 1843.
- 28. The method as recited in Claim 26, characterised in that Step e) is carried out by means of hybridisation of at least one oligonucleotide according to Claims 13 through 19.
- 29. The method as recited in Claim 26, characterised in that Step e) is carried out by means of hybridisation of at least one oligonucleotide according to Claims 13 through 19 and extension of said hybridised oligonucleotide(s) by means of at least one nucleotide base.
- 30. The method as recited in Claim 26, characterised in that Step e) is carried out by means of sequencing.

- 31. The method as recited in Claim 26, characterised in that Step d) is carried out using methylation specific primers.
- 32. The method as recited in Claim 26, characterised in that Step e) is carried out by means of a combination of at least two of the methods described in Claims 27 through 31.
- 33. The method as recited in Claim 26, characterised in that the treatment is carried out by means of a solution of a bisulfite, hydrogen sulfite or disulfite.
- 34. A method according to any one of Claims 1 to 3 comprising the following steps:
 - a) obtaining a biological sample containing genomic DNA,
 - b) extracting the genomic DNA,
 - c) digesting the genomic DNA comprising one or more of the sequences from the group consisting of SEQ ID Nos 83, 91, 90 and 27 and sequences complementary thereto with one or more methylation sensitive restriction enzymes, and
 - d) determining of the DNA fragments generated in the digest of step c).
- 35. The method according to Claim 34, characterised in that the target sequence or sequences digested in Step c) comprises one or more sequences from the group consisting of SEQ ID NO 122 to SED ID NO 135.
- 36. A method according to one of Claims 34 or 35, wherein the DNA digest is amplified prior to step d).
- 37. The method as recited in one of the Claims 26 through 33 and 36 characterised in that more than ten different fragments having a length of 100 200 base pairs are amplified.
- 38. The method as recited in one of Claims 26 through 33, 36 and 37 characterised in that the amplification of several DNA segments is carried out in one reaction vessel.
- 39. The method as recited in one of the Claims 26 through 33 and 36 through 38, characterised in that the polymerase is a heat-resistant DNA polymerase.

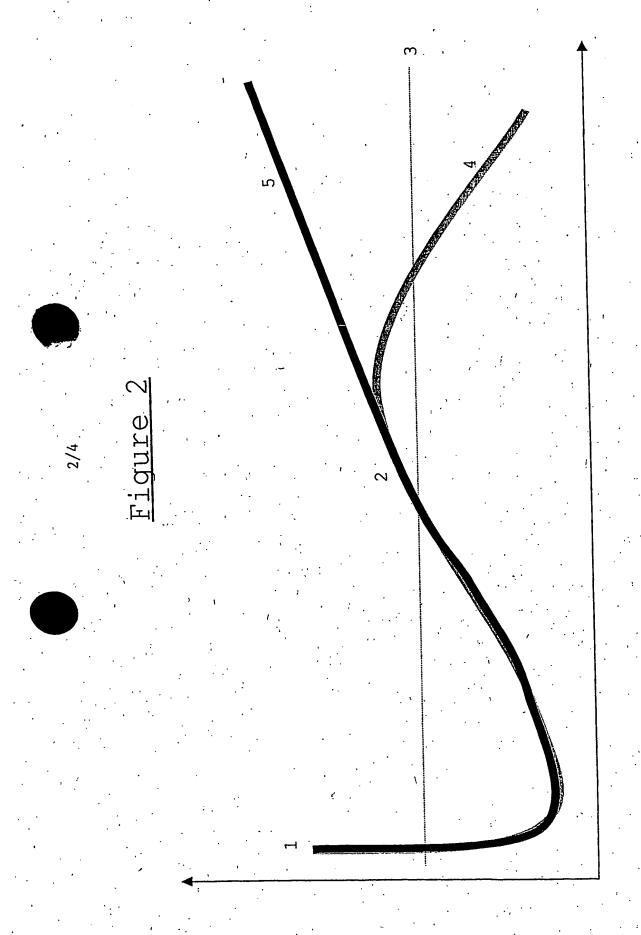
- 40. The method as recited in one of the Claims 26 through 33 and 36 through 39, characterised in that the amplification is carried out by means of the polymerase chain reaction (PCR).
- 41. The method as recited in one of the 26 through 33 and 36 through 40, characterised in that the amplificates carry detectable labels.
- 42. The method according to Claim 41 wherein said labels are fluorescence labels, radionuclides and/or detachable molecule fragments having a typical mass which can be detected in a mass spectrometer.
- 43. The method as recited in one of the Claims 26 through 33, characterised in that the amplificates or fragments of the amplificates are detected in the mass spectrometer.
- 44. The method as recited in one of the Claims 42 and/or 43, characterised in that the produced fragments have a single positive or negative net charge for better detectability in the mass spectrometer.
- 45. The method as recited in one of Claims 41 through 44, characterised in that detection is carried out and visualised by means of matrix assisted laser desorption/ionization mass spectrometry (MALDI) or using electron spray mass spectrometry (ESI).
- 46. The method as recited in one of the Claims 26 through 41, characterised in that the genomic DNA is obtained from cells or cellular components which contain DNA, sources of DNA comprising, for example, cell lines, histological slides, biopsies, tissue embedded in paraffin, breast tissues, blood, plasma, lymphatic fluid, lymphatic tissue, duct cells, ductal lavage fluid, nipple aspiration fluid, bone marrow and combinations thereof.
- 47. A kit comprising a bisulfite (= disulfite, hydrogen sulfite) reagent as well as oligonucleotides and/or PNA-oligomers according to one of the Claims 13 through 19.

- 48. A kit according to claim 47, further comprising standard reagents for performing a methylation assay from the group consisting of MS-SNuPE, MSP, Methyl light, Heavy Methyl, nucleic acid sequencing and combinations thereof.
- 49. The use of a method according to one of claims 1 through 11, 21, and 24 to 46, a nucleic acid according to Claim 12, of an oligonucleotide or PNA-oligomer according to one of the Claims 13 through 19, of a kit according to Claim 47 or 48, of an array according to one of the Claims 23 through 25 or of a set of oligonucleotides according to one of claims 16 through 19 for the treatment, characterisation, classification and/or differentiation, of breast cell proliferative disorders.

Abstract

The present invention relates to modified and genomic sequences, to oligonucleotides and/or PNA-oligomers for detecting the cytosine methylation state of genomic DNA, as well as to a method for predicting the response of a subject with a cell proliferative disorder of the breast tissues, to endocrine treatment.

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Sequence listing

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<212> DNA

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<220>

<223> chemically treated genomic DNA (Homo sapiens)

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                                                                   1440
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<210> 161 <211> 2501

<212> DNA

<213> Artificial Sequence

<220>

<223> chemically treated genomic DNA (Homo sapiens)

<400> 161 · ·

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<212> DNA

<213> Artificial Sequence

<220>

<223> chemically treated genomic DNA (Homo sapiens)

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<213> Artificial Sequence

<220>

<223> chemically treated genomic DNA (Homo sapiens)

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<220> <223> chemically treated genomic DNA (Homo sapiens)

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572 41

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<220>

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2340

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2580

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- 2640 2700

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<223> chemically treated genomic DNA (Homo sapiens)

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960

1020

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13> Artificial Sequence

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213> Artificial Sequence

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<220>

<223> chemically treated genomic DNA (Homo sapiens)

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<223> chemically treated genomic DNA (Homo sapiens)

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<211> 3862

<212> DNA

<213> Artificial Sequence -

<220>

<223> chemically treated genomic DNA (Homo sapiens)

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<211> 2358

<212> DNA

<213> Artificial Sequence

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<212> DNA

<213> Artificial Sequence

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<223> chemically treated genomic DNA (Homo sapiens)

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<211> 3780

<212> DNA

<213> Artificial Sequence

<220>

<223> chemically treated genomic DNA (Homo sapiens)

400> 287

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<213> Artificial Sequence

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<223> chemically treated genomic DNA (Homo sapiens)

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<211> 2515

<212> DNA

<213> Artificial Sequence

<220> ′

223> chemically treated genomic DNA (Homo sapiens)

400> 289

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<223> chemically treated genomic DNA (Homo sapiens)

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<213> Artificial Sequence

€220> -

223> chemically treated genomic DNA (Homo sapiens)

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(220>

223> chemically treated genomic DNA (Homo sapiens)

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213> Artificial Sequence

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<213> Artificial Sequence

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